

TSCA HEALTH & SAFETY STUDY COVER SHEET

TSCA CBI STATUS:

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Submit a sanitized cover sheet with CBI deleted. Mark the sanitized copy, "Public Display Copy" in the heading.

1.0 SUBMISSION TYPE *--Contains CBI*

8(d) 8(e) FYI 4 OTHER: Specify _____

XX- Intial Submission -Follow-up Submission -Final Report Submission

Previous EPA Submission Number or Title if update or follow-up:

8EHQ-0299-14394

Docket Number, if any: #

continuation sheet attached

2.1 SUMMARY/ABSTRACT ATTACHED

(may be required for 8(e); optional for §4, 8(d) & FYI)

X - YES

NO

2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID

Cert# P 917006757

99-2-13

2.3 FOR EPA USE ONLY

3.0 CHEMICAL/TEST SUBSTANCE IDENTITY *-Contains CBI*

Reported Chemical Name (specify nomenclature if other than CAS name):

CAS#: 111988-49-9

(Cyanamide, [3-(6-chloro-3-pyridinyl)methyl]-2]thiazolidinylidene]-,

Purity _____ %

X - Single Ingredient

Commercial/Tech Grade

Mixture

Trade Name: YRC 2894

Common Name: Chlornicotinyl

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99 FEB-14 AM 11:38

4.0 REPORT/STUDY TITLE *- Contains CBI*

Study on Acute Inhalation Toxicity in Rats According to OECD No. 403, Report # 24775

Continuation sheet attached

5.1 STUDY/TSCATS INDEXING TERMS

[CHECK ONE]

HEALTH EFFECTS (HE): X

ENVIRONMENTAL EFFECTS (EE):

ENVIRONMENTAL FATE (EF):

5.2 STUDY/TSCATS INDEXING TERMS (see instructions for 4 digit codes)

STUDY	SUBJECT	ROUTE OF	VEHICLE OF
TYPE: ATOX	ORGANISM (HE, EE only): RATS	EXPOSURE (HE only):	EXPOSURE (HEonly):
Other:	Other:	Other:	Other:

6.0 REPORT/STUDY INFORMATION *L Contains CBI*

X- Study is GLP

Laboratory: Bayer Toxicology, Wuppertal, Germany

Report/Study Date: 6/16/95

Source of Data/Study Sponsor (if different than submitter)

Number of pages : 123

continuation sheet attached

7.0 SUBMITTER INFORMATION *L Contains CBI*

Submitter: Donald W. Lamb, Ph.D Title: V. P., Prod. Safety & Reg. Affrs Phone: 412-777-7431

Company Name: Bayer Corporation Company Address: 100 Bayer Road

Pittsburgh, PA 15205-9741 Submitter Address (if different):

Technical Contact: Donald W. Lamb, Ph.D Phone: (412)777-7431

continuation sheet attached

8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS *L Contains CBI*

This compound is a developmental insecticide.



8EHQ-99-14394

continuation sheet attached

Submitter Signature: Donald W. Lamb Date: 2/1/99

99 APR-8 AM 10:47

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88990000113

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9.0 CONTINUATION SHEET

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P917006757
99-2-13

CONTINUED FROM COVER SHEET SECTION # 2.1

The clinical sign of reduced motility occurred in more than two animals with the duration of the sign being greater than two days. As this clinical finding occurred in more than two non-moribund animals with the finding lasting for more than two days, this finding is a trigger for reporting. Also, the LC50 in females of 1223 mg/m³ triggers reporting.

Abstract

The acute inhalation toxicity of YRC 2894 was evaluated in male and female Wistar rats. Groups of rats were exposed to a solid aerosol (dust) average concentration of 80, 481, 1523, and 2535 mg/m³ of air.

Concentrations up to and including 481 mg/m³ of air did not induce test compound-related mortality. Exposure to 1523 and 2535 mg/m³ of air was tolerated without mortality in males, but produced mortality in females. Mortality occurred from post-exposure day one through seven. Necropsy findings support the conclusion that a causal relationship between lethality and lung damage existed. Exposure to concentrations of 481 mg/m³ of air and higher were followed by a concentration-dependent bradypnea, dyspnea, labored breathing pattern, rales, nose/snout area with red encrustations, salivation, prostration (lying on side or belly), blepharospasm, mydriasis, chromodacryorrhea, tremor, reduced motility, apathy, hair coat ungroomed, hypothermia, decrease in body in body weight, and piloerection. The duration of clinical signs (maximum duration up to day 6) was dependent on respiratory signs.

The LC50 for males was > 2535 mg/m³ of air, and the LC50 for females was approximately 1223 mg/m³ of air.

STUDY TITLE

YRC 2894
Study on Acute Inhalation Toxicity
in Rats According to OECD No. 403

DATA REQUIREMENT

108856

US EPA-FIFRA Guideline No. 81-3

AUTHOR

Priv.-Doz. Dr. J. Pauluhn

FILE

8761

STUDY COMPLETION DATE

June 16, 1995

PERFORMING LABORATORY

BAYER AG
DEPARTMENT OF TOXICOLOGY
Friedrich-Ebert-Strasse 217-233
D-42096 Wuppertal
Germany

LABORATORY PROJECT ID

Bayer AG Report No. 24775
Bayer AG Study No. T5058291

STATEMENT OF DATA CONFIDENTIALITY

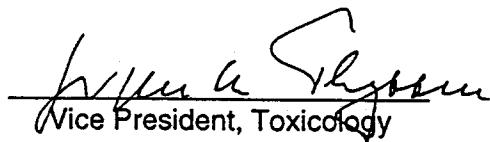
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The following statement supercedes the above statement of confidentiality that may occur elsewhere in this report:

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA Section 10(d)(1)(A), (B), or (C).

BAYER CORPORATION

Dr. J.H. Thyssen:


Vice President, Toxicology

Date:

Jan. 26, 99

GOOD LABORATORY PRACTICE STATEMENT

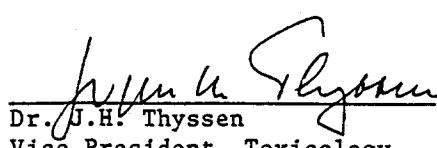
This study was conducted in compliance with the OECD Principles of Good Laboratory Practice (GLP) and with the Principles of Good Laboratory Practice (GLP) according to Annex 1 ChemG (1994, cf. references) and meets the FIFRA Good Laboratory Practice Standards (40 CFR Part 160), with the exception that recognized differences exist between the GLP principles/standards of OECD and FIFRA (for instance, authority granted Agency inspectors and certain record retention requirements).


Dr. J. Pauluhn D.A.B.T.
Board Approved Toxicologist (DGPT)
Study Director

Date: Jan 16, 95


Prof. Dr. E. Löser
Head of Institute

Date: 18. Juli 1995


Dr. J.H. Thyssen
Vice President, Toxicology

Date: Jan. 26, 99

SUBMITTER:
BAYER CORPORATION

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2. QUALITY ASSURANCE STATEMENT

Test Substance: YRC 2894

Study No.: T5058291

The study was audited by Quality Assurance on the dates given below. Audit reports have been submitted in writing to the study director and, if necessary, also the laboratory management, or other persons affected.

Date of audit	Date of report to study director/management
Sep. 16, 1994 (study plan)	Sep. 16, 1994
Sep. 21, 1994	Sep. 21, 1994
Oct. 05, 1994	Oct. 05, 1994

To the best of my knowledge, the results of the study and the methods used have been correctly reported.

Quality Assurance Unit
PH-QA-C/GLP, Bayer AG

Date:

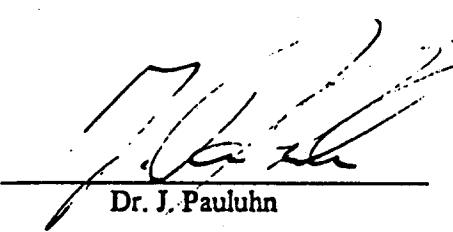
Feb. 05, 1996

Responsible:

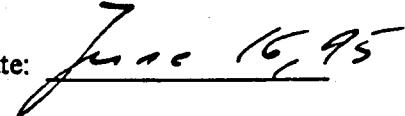
R. Rauchschwalbe
Dr.R.Rauchschwalbe

3. SIGNATURES

Study
Director:


Dr. J. Pauluhn

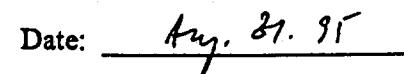
Date:


June 16, 95

Institute
Head:


Prof. E. Löser

Date:


Aug. 21, 95

4. SUMMARY

A study on the acute inhalation toxicity of YRC 2894 (hereafter referred to as *test substance*) in rats has been conducted in accordance with OECD Guideline No. 403. Groups of rats were exposed to a solid aerosol (dust) average concentration of 80, 481, 1523, and 2535 mg/m³ air. Attempts were made so that aerosol generated was respirable to rats. The results can be summarized as follows:

LC₅₀ inhalation (aerosol, 4 hr) Males: > 2535 mg/m ³ ¹⁾ Females approx. 1223 mg/m ³	NO(A)EL Males & Females: 80 mg/m ³ air ¹ .
--	--

Observations and Measurements

Aerosol (dust) concentrations up to and including 481 mg/m³ did not induce test substance related mortality. Exposure to 1523 and 2535 mg/m³ test compound was tolerated without mortality in males but produced mortality in females. Mortality occurred from postexposure day one through seven. Necropsy findings support the conclusion that a causal relationship between lethality and lung damage existed. Exposures to concentrations of 481 mg/m³ and higher were followed by a concentration-dependent bradypnoea, dyspnoea, laboured breathing pattern, rales, nose/snout area with red encrustations, salivation, prostration (lying on side or belly), blepharospasm, mydriasis, chromodacryorrhea, tremor, reduced motility, apathy, haircoat ungroomed, hypothermia, decrease in body weights, and piloerection. The duration of signs (maximum duration up to day 6) was dependent on respiratory signs.

The aerosol generated was of adequate respirability in the lower exposure groups (i.e. MMAD ca. 3 µm, GSD ca. 1.7, relative mass < 3 µm ca. 49%). It appeared not feasible to generate concentrations exceeding 500 mg/m³ air using a cyclone. This, in fact, resulted in a decreased respirability of particles. Despite the lower respirability rats died in the higher exposure groups.

Evaluation and Assessment

The aerosolized test substance (dust) proved to have a moderate acute inhalation toxicity to rats. Cumulative evidence suggest that there is a causal relationship of local effects to the respiratory tract and the observed findings.

¹ All concentration data represent gravimetical concentrations of the test substance in the rats' breathing zone.

5. INTRODUCTION

This acute inhalation toxicity study was conducted in accordance with OECD Guideline No. 403 using YRC 2894 as a test substance. The study was performed on rats (nose-only exposure over 4 hours to a solid aerosol, dynamic exposure conditions, 2 week observation period). This study served the purpose of product classification and to estimate the potential acute health hazard resulting from handling this product.

The study was conducted at the test facility of the Institute of Toxicology, Department of Toxicology, Bayer AG, D-42096 Wuppertal, Germany.

Study No.: T5058291

Study period: September 21, 1994 - October 13, 1994

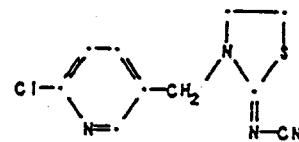
6. RESPONSIBILITIES

Head of Department: Prof. Dr. E. Löser
Study Director and Report Author: Dr. J. Pauluhn
Biometric evaluation: Dr. J. Pauluhn
Test substance delivery: Dr. Großmäder
Test substance / supply of analytical data: Dr. W. Gau
Central Animal Supply Department: Dr. K. Hoffmann
Air conditioning/air make-up Dipl. Ing. G. Strietholt
Archiving the study data: Prof. G. Schlüter
Quality Assurance: Dr. H. Lehn
Gross pathology: Dr. Rosenbruch

7. MATERIALS AND METHODS

7.1. Test Substance

Test substance: YRC 2894
Synonym: NTN 33894
Indication: insecticide
Purity: 97.2 % (see Appendix)
Producer: Bayer AG, Leverkusen, Germany
Stability: guaranteed for the duration of this study
Appearance: white-yellowish powder
Storage: Room temperature / darkness
Chemical name: 3-(2-Chlor-5-pyridylmethyl)-2-cyaniminothiazolidin
CAS-no.: --
Molecular weight: 252.5 g/mol
Empirical formula: C₁₀H₉ClN₄S



7.2. Test System and Housing of Animals

Species and species justification: The study was carried out in rats, a rodent species recommended in the test guidelines.

Healthy young adult SPF bred Wistar rats, strain Hsd/Win:WU [formerly BOR: WISW (SPF-Cpb)], from the experimental animal breeder Harlan-Winkelmann, Borch, Germany, were used. Animals of this strain have been used at Bayer AG in toxicological studies for years. Historical data on their physiology, diseases and spontaneous alterations are available. The state of health of the strain is randomly checked regularly at the instance of the Central Animal Supply Department, Bayer AG, for the most important specific infectious pathogens. The results of these examinations are archived.

Acclimatization: The animals were acclimatized to the animal room conditions for at least 5 days before use.

Identification: Animals were identified by both individual color-marking and cage-labels. All animals from this study were located on one cage-rack.

Randomization: Before the start of the study the health status of each animal was assessed. Animals were subsequently assigned to exposure groups at random (randomization procedure is described in section 7.17).

Health status: Only healthy rats free of signs were used for this study. The animals were not vaccinated or treated with anti-infective agents either before their arrival or during the acclimatization or study periods. The females were nulliparous and not pregnant.

Age and weight: At the study start the variation of individual weights did not exceed ± 10 per cent of the mean for each sex (see Appendix). Animals of the weight class used are 2 - 3 months old and hence fulfill the criterion for young adults.

Animal housing: During the acclimatization and study periods the animals were housed singly in conventional Makrolon® Type II cages (based on A. Spiegel and R. Gönnert, Zschr. Versuchstierkunde, 1, 38 (1961) and G. Meister, Zschr. Versuchstierkunde, 7, 144-153 (1965)). Cages and water bottles were changed twice a week while unconsumed feed was changed once per week. The legal requirements for housing experimental animals (86/609 EEC) were followed.

Bedding: Bedding consisted of type S 8/15 low-dust wood granulate from Ssniff, Soest/Westfalen, Germany. The wood granulate was randomly checked for harmful constituents at the request of the Central Animal Supply Department, Bayer AG.

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Animal rooms: All animals were housed in a single room. For reasons of space availability rats from other acute toxicity studies were housed in the same room, however mistakes in animal assignments were excluded by adequate spatial separation, clear cage labeling, and appropriate organization of all work procedures. The housing of several studies in one animal room is not considered to be a deviation from current GLP-requirements since many acute studies comprise of 10 animals only (as required to perform a limit test).

Environmental Conditions in the Animal Room

The animal room environment was as follows:

Room temperature:	22 ± 2 °C
Relative humidity:	approximately 50 %
Dark/light cycle:	12 h/12 h; artificial light from 6.00 a.m. to 6.00 p.m. Central European Time
Light intensity:	approximately 14 watt/m ² floor area
Ventilation:	approximately 10 air changes per hour

The room humidity and temperature were continuously monitored and documented using a calibrated thermohygrograph. Occasional deviations from these conditions occurred, e.g. as a result of animal room cleaning, but these had no detectable influence on the outcome of this study.

Cleaning, disinfection, and pest control: The animal room was regularly cleaned and disinfected once a week with an aqueous solution of Zephirol®. Contamination of the feed and contact with the test system were excluded. Pest control was not conducted in the animal room.

Feeding: Ration consisted of a standard fixed-formula diet (Altromin® 1324 pellets maintenance diet for rats and mice, Altromin GmbH, Lage) and tap water (drinking bottles). Both food and water were available *ad libitum*. The pelletized feed was contained in a rack in the stainless-steel wire cage cover. The nutritive composition and contaminant content of the standard diet was checked regularly by random sampling by the Central Animal Supply Department, Bayer AG. Details concerning general feed and water specifications are provided in the Appendix.

Water: Drinking quality tap-water (Drinking Water Decree of 05.12.1990, Bundesgesetzblatt [federal law gazette] part I, page 2612) was provided *ad libitum* in polycarbonate bottles containing approximately 300 ml (based on A. Spiegel and R. Gönnert, Zschr. Versuchstierkunde, 1, 38 (1961) and G. Meister, Zschr. Versuchstierkunde, 7, 144-153 (1965)). The results of feed and water analyses are retained by Bayer AG. The available data provided no evidence of an impact on the study objective.

7.3. Test Guidelines

The study described below was carried out in accordance with OECD Guideline No. 403. The study conditions were adjusted so as to fulfill both the EC Guideline 92/69/EEC and the FIFRA § 81-3 (US EPA, 1984) guideline. Other recommendations (US EPA, 1988) were also considered so as to comply with internationally recognized procedures.

7.4. Exposure Conditions

Mode of exposure: Animals were exposed to the aerosolized test substance in Plexiglas exposure tubes applying a *directed-flow* nose-only exposure principle. Tubes were chosen that accommodated the animals size. These tubes were designed so that the rat's tail remained outside the tube, thus restrained-induced hyperthermia can be avoided. This type of exposure is preferable to whole-body exposure on scientific (Pauluhn, 1984) and technical reasons (rapid attainment of steady-state concentrations, no problems with regard to test atmosphere inhomogeneities, better capabilities to control all inhalation chamber parameters, easier cleaning of exhaust air, and lower consumption of test substance). Moreover, contamination of the fur can largely be avoided. The chambers used are commercially available (TSE, 61348 Bad Homburg) and the performance of this type of chamber has been published (Pauluhn, 1984; Pauluhn, 1988; Pauluhn, 1994).

Vehicle: The test substance was aerosolized as dust without a carrier or vehicle.

7.5. Aerosol Generation and Exposure Technique

Aerosol generation: Under dynamic conditions the test substance was fed into the intake of the cylindrical inhalation chamber shown in figure 1.

In order to obtain the high concentration of respirable aerosol an EXACTOMAT 4200 (TSE, 61348 Bad Homburg, Germany) and for the lower concentration a Wright-Dust-Feeder (BGI Inc., Waltham, MA, USA) was used (for details cf. Table 1 in the result section).

Wright-Dust-Feeder: For powder dispersion, conditioned compressed air (28 liters of air/min) was used. Under continuous *dynamic* generation conditions the test substance was entrained into the inner compartment of the inhalation chamber so as depicted in Figure 1.

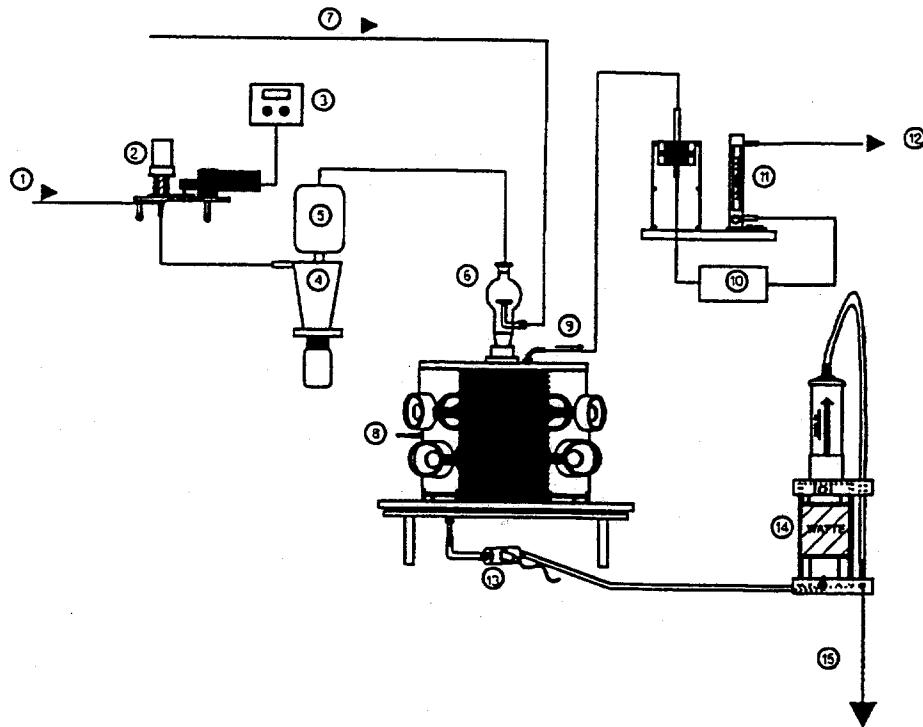
Exactomat: For the generation of higher powder concentrations the Exactomat dust generator was used (conditioned compressed air, 28 liters of air/min; continuous operation). The principle performance of the dust generating system can be described as follows: The test substance was entrained into a glass reservoir. From this reservoir it was fed (by suction) into the orifice of a venturi tube. The airborne powder was then dispersed into the inner cylinder of the inhalation chamber depicted in Figure 1. Reproducible and temporally stable dosing into the orifice of the venturi tube was achieved by an oscillating orifice. The orifice size was adjusted manually in order to obtain the targeted flow of powder. Stirring of the reservoir was performed using a minimum number of revolutions per unit of time. Thus the flowability of the

test compound was maintained without inducing a vertical inhomogeneity of active ingredient particles.

Optimization of respirability: In order to increase the efficiency of the generation of respirable particles and prevents larger particles from entering the chamber a cyclone was used (Tillery et al., 1976). Previous experience with cyclones have demonstrated that this device could only be used up to concentrations of 500 mg/m³ air.

Inhalation Chamber: The aluminum inhalation chamber has the following dimensions: inner diameter = 14 cm, outer diameter = 35 cm (two-chamber system), height = 25 cm (internal volume = about 3.8 l). The construction of the inhalation chamber is shown schematically in Fig. 1. Details of this modular chamber and its validation with regard to spatial homogeneity of material distribution have been published (Pauluhn, 1994).

Fig. 1: Inhalation Chamber



- | | |
|--|---|
| 1. Compressed air supply
2. Dust generator (Wright-Dust-Feeder)
3. Digital control unit
4.-5. Cyclone
6.-7. Dilution unit (not used)
8. Sampling location ('breathing zone sampling') | 9.-12. Real-time monitoring
13. Sensor for temperature and humidity measurement
14. Cotton-wool aerosol filter + HEPA filter
15. Exhaust air |
|--|---|

Conditioning the compressed air: Compressed air was supplied by Boge compressors and was conditioned (i.e. freed from water, dust, and oil) automatically by a VIA compressed air dryer. Adequate control devices were employed to control supply pressure.

Inhalation chamber steady-state concentration: The test atmosphere generation conditions provide an adequate number of air exchanges per hour (> 400 x, continuous generation of test atmosphere). Under such test conditions steady state is attained within the first minute of exposure ($t_{99\%} = 4.6 \times \text{chamber volume}/\text{flow rate}$; McFarland, 1976). The ratio between the air supplied and exhausted was chosen so that approximately 90% of the supplied air is removed as exhaust. The remainder provides adequate dead-space ventilation for the exposure tubes. At each exposure port a minimal air flow rate of 1.4 l/min was provided. This is equivalent to approximately 4 respiratory minute volumes of the rats. The test atmosphere can by no means be diluted by bias-air-flows. The inhalation chamber was operated in a well ventilated chemical fume hood.

Air flows: During the exposure period air flows were monitored continuously and, if necessary, readjusted to the conditions required. Air flows were measured with calibrated flowmeters and/or soap bubble meter (Glibrator, Ströhlein Instruments, Kaarst) and were checked for correct performance at regular intervals.

Treatment of exhaust air: The exhaust air was purified via cotton-wool/activated charcoal and HEPA filters. These filters were disposed of by Bayer AG.

7.6. Inhalation Chamber Temperature and Humidity

The temperature and humidity measurements were made using a computerized system (Leybold Heraeus). The values were recorded at intervals of 10 min. For technical reasons the test atmosphere temperature and humidity were measured from the exhaust flow. Details of this monitoring system have been reported elsewhere (Pauluhn, 1986).

The relative humidity was measured with a humidity sensor (CCH capacitor). The humidity-sensor is protected from particles by a double sintered metal filter with an interposed Teflon membrane (pore size approximately 1 μm). This sensor was calibrated using saturated salt solutions according to Greenspan (1977). The temperature sensors were calibrated with a calibration thermometer. The measured values were recorded and evaluated with an Apple 2e computer and an MDP 8240/45 analogue-digital converter using an IEEE 488 interface.

7.7. Analysis of the Test Atmosphere

A nominal concentration was not calculated since the construction and weight of the dust generator used did not allow for a precise measurement of the powder aerosolized.

Gravimetric evaluation: The test-substance concentration was determined by gravimetric analysis (filter: Cellulose-Acetate-Filter, Sartorius, Göttingen, Germany; balance: Mettler AE 100).

Chamber samples were taken in the vicinity of the breathing zone (see Fig. 1). The number of samples taken was sufficient to characterize the test atmosphere and was adjusted so as to accommodate the sampling duration and/or the need to confirm specific concentration values. Optimally, samples were collected after the equilibrium concentration had been attained in hourly intervals. All analytical concentrations reported refer to mg of test substance/m³ air (gravimetical method).

7.8. Characterization of Aerodynamic Particle-Size Distribution

The samples for the analysis of the particle-size distribution were also taken in the vicinity of the breathing zone.

The particle-size distribution was analyzed using cascade impactors. Specifications and evaluations are provided in the Appendix. The individual impactor stages had been subjected to gravimetric analysis. An adhesive stage coating (silicone spray) was used to prevent particle bounce and re-entrainment, respectively. The glass stage (Andersen type of impactor) or the aluminum foil covering the stage (Berner) type of impactor) were evaluated gravimetrically.

Evaluation of particle-size distributions: For the evaluation of the cascade impactor analyses the mass median aerodynamic diameter (MMAD) and the geometric standard deviation (GSD) are determined from the probit-transformed cumulative particle mass frequency distribution (y-axis) and the logarithmic effective cut-off diameters (ECD's) (x-axis) of the individual impactor stages by linear regression. The GSD is calculated from the regression line: percentile 84 / percentile 50. The relative mass with an aerodynamic diameter $\leq 3 \mu\text{m}$ ("respirable mass fraction") [Raabe, 1982; Snipes, 1989; SOT-Commentary, 1992] is calculated from the regression line. For probit transformation and linear regression FORTRAN algorithms published by Rosiello et al. (1977) are used. The MMAD was calculated using published following formulas [Marple and Rubow, 1980; Pauluhn, 1994].

To verify whether the aerosol distribution is in fact unimodal and log-normal the normalized mass per stage (f'_H) is evaluated as a histogram. $\Delta \log D_p$ is equal the difference $\log D_{p+1} - \log D_p$, whereas D_p is the lower (left) cut-size limit and D_{p+1} the higher (right) cut-size limit of the corresponding impactor stage. As demonstrated by the evaluations included in the Appendix, the impactor stage cut-off limit (D_{p+1}) to the right was used for all calculations.

$$f'_H = \frac{1}{N_f} \times \frac{\text{mass / stage}}{\Delta \log D_p}$$

The log-normal mass distribution $y'(D_{ae}) = 1/N_f \times y(D_{ae})$ as a function of the aerodynamic diameter (D_{ae}) is computed using the formula:

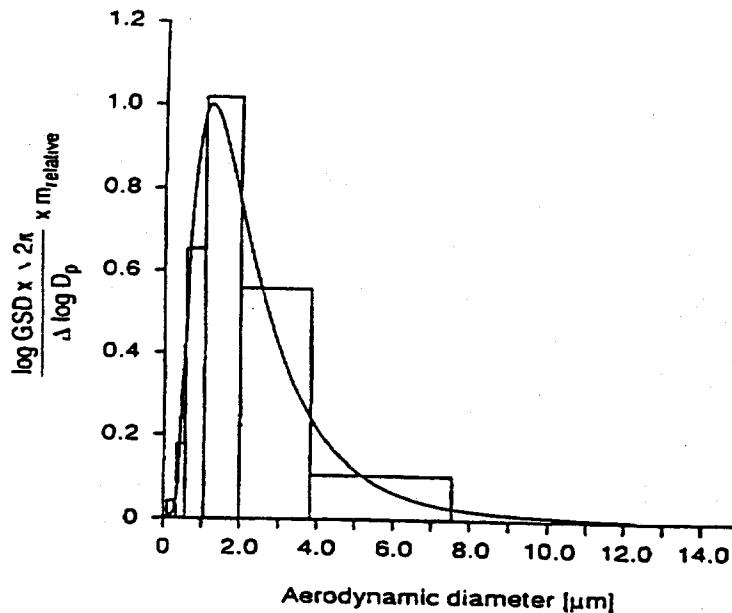
$$y'(D_{ae}) = \exp\left(-\frac{(\log D_{ae} - \log \text{MMAD})^2}{2 \times \log^2 \text{GSD}}\right)$$

The normalization factor (N_f) is calculated as follows:

$$N_f = \frac{\Sigma \text{mass}}{\log GSD \times \sqrt{2\pi}}$$

Where Σmass is the total mass collected by the cascade impactor, where $m_{\text{relative}} = \text{mass per stage}/\Sigma \text{mass}$ (cf. Fig. 2).

Figure 2: Principle of characterization of aerosol atmosphere



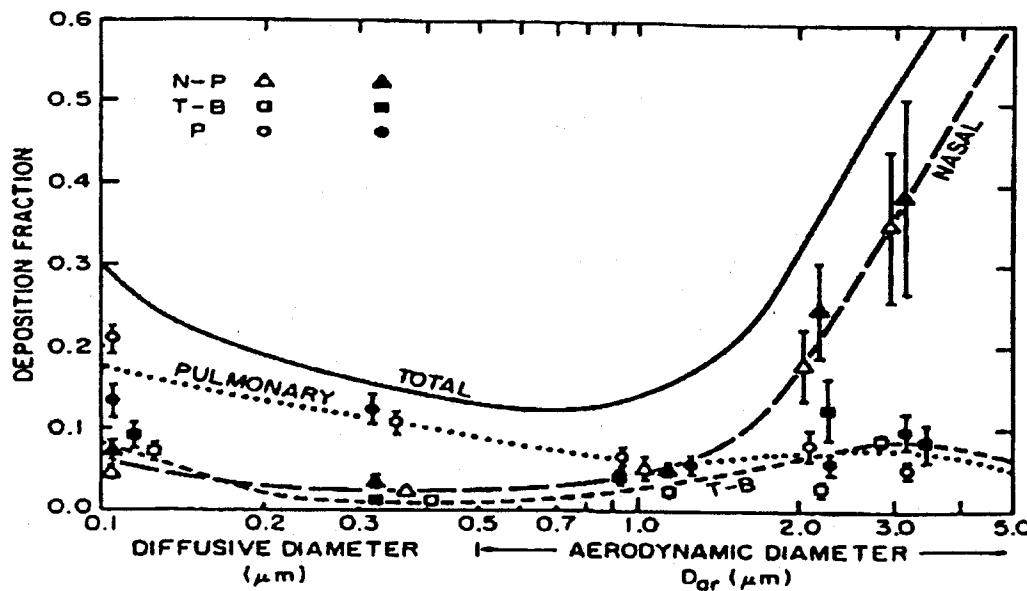
Where Σmass is the total mass collected by the cascade impactor, where $m_{\text{relative}} = \text{mass per stage}/\Sigma \text{mass}$.

The algorithm for the calculation of particle size characteristics is taken from pertinent reference works on aerosol physics (Dennis, 1976; Marple and Rubow, 1980) and proves to be generally applicable (Pauluhn 1988; Pauluhn, 1994).

Respirability

Fig. 3 below, demonstrates that the particle size distribution achieved is adequate to reach all potential target structures of the respiratory tract.

Fig. 3 Respirability of Aerosols (Raabe, 1982)



7.9. Collection Efficiency

The sampling equipment was adjusted with calibrated rotameters to internationally recognized standards (ACGIH, 1978; Section I "Calibration of Air Sampling Instruments").

The conditions for generating the test atmosphere are optimized to provide maximum aerosol respirability to rats (Raabe, 1982; Snipes, 1989; SOT-Commentary, 1992). The absence of larger particles and high flow rates in the vicinity of the sampling ports make it possible to disregard potential anisokinetic sampling errors, thus ensuring a representative sampling even with different sampling probe orifice diameters and flow rates. The tolerance limits for the radius of the probe orifice are calculated using the following formula [ACGIH, 1978]. Calculations consider both a particle size distribution that encompasses aerodynamic diameters (D_{ae}) of 0.5 to 7.4 μm and sample flows ranging from 8 to 80 ml/sec.

$$5 \times \sqrt[3]{\frac{\text{flow} \times \tau}{4 \times \pi}} \leq r_p \leq \frac{1}{5} \times \sqrt[3]{\frac{\text{flow}}{g \times \tau \times \pi}}$$

r_p = radius of the sample probe in cm = $\frac{1}{2} \times D_p$

τ = relaxation time ($D_{ae} 0.5 \mu\text{m} = 1 \times 10^{-6} \text{ sec}$; $D_{ae} 7.4 \mu\text{m} = 1.7 \times 10^{-4} \text{ sec}$)

g = gravity constant = 980 cm/sec²

Tolerance limits calculations for the sample probe orifice (r_p) indicated that a representative sampling is assured when the orifice inner diameter is in the range of 1.0 to 1.6 cm. Orifices of the sampling instruments used here are in compliance with this criteria. Details of the D_p tolerance limit calculations are published elsewhere (Pauluhn, 1988; Pauluhn, 1994).

7.10. Stability of the Test Atmosphere

Attempts were made (pilot study) to monitor the integrity and stability of the aerosol generation system using a RAS-2 aerosol photometer (MIE, Bedford, Massachusetts, USA). However, the particle number-concentration was too high to allow a reliable monitoring of the atmosphere produced.

7.11. Number of Animals

Five male and five female rats were simultaneously exposed to each concentration under nose-only conditions for 4 h.

7.12. Control Animals

To identify exposure-related effects, comparisons with appropriate controls are conducted. Controls were exposed to conditioned air using almost similar exposure conditions as were used for the test substance (15 liters air/min; duration of exposure = 1 x 4 h; 5 males and females per group; 4 week observation period). Direct comparisons were made between the control and exposure groups.

Note: Control studies are performed under GLP-conditions but without assignment to a particular study. This allows use of control data for several studies that have been performed under similar experimental conditions within a recent time frame. This procedure is in compliance with current testing guidelines as well as animal welfare regulations.

7.13. Body Weights and Duration of Observation Period

Body weights were measured before exposure, on days 3 and 7, and weekly thereafter. Individual weights are also recorded at death, if applicable. The period of observation was for a minimum of 2 weeks.

7.14. Clinical Signs

The appearance and behavior of each rat was examined carefully several times on the day of exposure and twice daily thereafter. Weekend assessments were made once a day (morning). Assessments from restraining tubes were made only if unequivocal signs occurred (e.g. spasms, abnormal movements, severe respiratory signs). Following exposure, observations are made and recorded systematically; individual records are maintained for each animal. Cageside observations included, but were not limited to, changes in the skin and fur, eyes, mucous membranes, respiratory, circulatory, autonomic and central nervous system, and somatomotor activity and behavior pattern. Particular attention was directed to observation of tremors, convulsions, salivation, diarrhea, lethargy, somnolence and prostration. The time of death is recorded as precisely as possible, if applicable.

Since these signs can only be assessed adequately from freely moving animals, no specific assessment was performed during exposure while animals were restrained.

Clinical observations were conducted so as to take into account the pattern of examination consistent with a Functional Observational Battery (FOB). Each rat was first observed in its home cage and then individually examined. The following reflexes were tested, based on recommendations made by Irwin (1968) and Moser et. al. (1988): visual placing response and grip strength on wire mesh, abdominal muscle tone, corneal and pupillary reflexes, pinna reflex, righting reflex, tail-pinch response, startle reflex with respect to behavioral changes stimulated by sounds (finger snapping) and touch (back).

7.15. Rectal Temperatures

The rectal temperatures were measured directly after cessation of exposure (approximately within ½ hour after the end of exposure) using a Digimed H 11 digital thermometer with an F2 rectal probe.

7.16. Necropsy

All surviving rats were sacrificed at the end of the observation period using sodium pentobarbital (Nembutal®) (approximately 300 mg/kg body weight, intraperitoneal injection). All rats, irrespective of the day of death, were given a gross-pathological examination. Consideration was given to performing a gross necropsy on animals as indicated by the nature of toxic effects, with particular reference to changes related to the respiratory tract. All gross pathological changes were recorded and evaluated.

7.17. Statistical Evaluation of Data

With graphs of means of data, the indicated parameters were evaluated relative to controls (mean = 100%). The single standard deviations are also shown relative to the means of the

controls. Statistically significant differences (versus control) are indicated here by asterisks ('*' for $p < 0.05$ and '**' for $p < 0.01$).

Necropsy findings: If specific findings occur from the respiratory tract of surviving rats they are evaluated statistically using the pairwise Fisher test after the R x C chi-squared test (HP 3000, Department of Toxicology, Bayer AG). The Fisher test was only performed if differences occurred between groups in the R x C chi-squared test or if a frequency value of < 5 was calculated. This procedure was performed in accordance with Gad and Weil (1982). For calculation of the unilateral p value a symmetrical distribution was assumed ($p_{\text{unilateral}} = (p_{\text{bilateral}})/2$).

Body weights: Means and single standard deviations of body weights are calculated. Mean body weights are also depicted graphically as a function of time (see Appendix). Since in acute studies individual group means may differ prior to commencement of the first exposure, the body weight gain was statistically evaluated for each group. For these evaluations a one-way ANOVA (vide infra) is used.

Particle size analysis: The statistical methods used in the evaluation of the particle-size distribution were described in Section 7.8.

Physical measurements: The means and, if appropriate (more than 3 values per measurement), a single standard deviation are calculated.

Physiological data: Data of rectal temperature measurements are statistically evaluated using the ANOVA procedure (vide infra).

Calculation of the LC₅₀: If calculation of a median lethal concentration (LC₅₀) is possible, it is performed by computer (HP 3000) according to the method of A.P. Rosiello, J.M. Essigmann, and G.N. Wogan (1977) as modified by Pauluhn (1983). This method is based on the maximum-likelihood method of C.I. Bliss (1938). If only 2 pairs of values with greater than 0% lethality and less than 100% are available then the first linear approximation is based on these values and a χ^2 -homogeneity test is not performed. The interpolated concentration at 50% lethality in this case was designated the approximate LC₅₀.

Randomization: A computerized list of random numbers served the purpose to assign animals at random to the treatment groups.

Analysis of variance (ANOVA): This parametric method checks for normal distribution of data by comparing the median and mean. The groups are compared at a confidence level of $(1-\alpha) = 95\%$ ($p = 0.05$). The test for the between-group homogeneity of the variance employed Box's test if more than 2 study groups were compared with each other. If the above F-test shows that the intra-group variability is greater than the inter-group variability, this is shown in the Appendix as "*no statistical difference between the groups*". If a difference is found then a pairwise post-hoc comparison is conducted (1- and 2-sided) using the Games and Howell modification of the Tukey-Kramer significance test. This program was originally

obtained from BCTIC.

7.18. Programming and Validating Software

Software code for the following purposes was written in HP Fortran (HP 3000) or Microsoft Fortran 77 (PC): particle-size analysis, ANOVA, Fisher test, inhalation chamber and physiological data tabulation program, graphics software. All scratch files were generated using Fortran F8.3 format using the Fortran default rounding routines. Fortran format A was always used to generate alphanumeric tables and graphs; i.e. numbers in figures and tables are rounded-up or -off due to the different format codes of the server. The computer programs were carefully validated. The validation was conducted using published text book data sets (e.g. BCTIC, Gad and Weil, 1982). However, it should be emphasized that the formal GLP-requirements required for software validation were not fulfilled. Wherever possible, raw data and calculated/derived values are displayed graphically to provide a versatile opportunity for data comparison.

7.19. Archiving the Raw Data and the Report

The protocol, raw data, and the final report are archived in locations specified by Bayer AG, in accordance with GLP requirements.

8. RESULTS

8.1. Generation and Characterization of Atmosphere

Technical information concerning generation of test atmospheres is provided in Table 1.

Table 1: Generation and characterization of chamber dust atmosphere

	Group 1	Group 2	Group 3	Group 4	Group 5
Generator	-	WDF	WDF	EXA	EXA
Gravimetric Conc. (mg/m ³)	Air control	80	481	1523	2535
Inlet Air Flow (l/min)	15	28	28	28	28
Exhaust Air Flow (l/min)	13	25	25	25	25
Temperature (mean, °C)	24	23	23	23	24
Rel. Humidity (mean, %)	16	10	16	30	38
MMAD (μm)	-	3.1	3.1	5.8	9.1
GSD	-	1.7	1.7	3.5	2.4
Aerosol Mass < 3 μm (%)	-	49	48	31	10
mass recovered (mg/m ³)	-	82	423	1012	2435

MMAD = Mass Median Aerodynamic Diameters

GSD = Geometric Standard Deviation.

- = not applicable

WDF: Wright-Dust-Feeder, EXA: Exactomat

For specific information concerning calculations of aerosol MMAD, GSD, and mass dependent size fraction below 3 μm, see the Appendix.

Characterization of the test atmospheres: Analytical monitoring of the aerosol test atmosphere from the breathing zone (3 samples/exposure) indicated that the exposure conditions were temporally stable over the exposure period. Analysis of the aerosol particle-size distribution from the breathing zone demonstrated that the aerosols generated were, in general, in the respirable/inspirable range when the Wright-Dust-Feeder/Cyclone-system was used. Concentrations exceeding 500 mg/m³ air were generated using the Exactomat without cyclone. This, in fact, resulted in a decreased respirability of particles. Despite the lower respirability rats died in the higher exposure groups.

Temperature values in the inhalation chamber were in the range suggested by the testing guidelines. Humidity values were lower; this is undoubtedly related to the use of dry air for generation. However, this deviation from the guideline has no negative impact on the study results.

8.2. Toxicological Results

The results obtained during and after exposures of rats for 4 h to this test substance are summarized in Table 2.

Table 2: Summary of acute inhalation toxicity

Group /sex	Gravimetric Concentration (mg/m ³)	Toxicological Result	Onset and Duration of Signs	Rectal Temperature (°C)	Onset of Mortality (%)
1 / m	0	0 / 0 / 5	--	38.3	--
2 / m	80	0 / 0 / 5	--	36.8*	--
3 / m	481	0 / 5 / 5	4h - 2d	34.6**	--
4 / m	1523	0 / 5 / 5	4h - 6d	33.2*	--
5 / m	2535	0 / 5 / 5	4h - 4d	32.7**	--
1 / f	0	0 / 0 / 5	--	38.2	--
2 / f	80	0 / 0 / 5	--	37.5	--
3 / f	481	0 / 5 / 5	4h - 2d	34.2**	--
4 / f	1523	3 / 5 / 5	4h - 4d	32.6**	1d - 2d
5 / f	2535	4 / 5 / 5	4h - 6d	33.7**	1d - 7d

m = males, f = females, -- not applicable

Values given in the 'Toxicological results' column are:

1st = number of dead animals.

2nd = number of animals with signs after cessation of exposure.

3rd = number of animals exposed.

Mortality / LC₅₀ Calculation:

LC₅₀ - males: > 2535 mg/m³ air

LC₅₀ - females: approximatively 1223 mg/m³ air

Figures addressing the LC₅₀-calculation are provided in the Appendix. From the survival curves it is evident that mortality occurred during postexposure days one through seven. Individual data addressing the time of death are provided in context with the necropsy data and incidence tables in the Appendix.

Signs and observations:

Details concerning signs and observations are provided in the Appendix as various incidence tables. The following list of signs is focusing on major signs only.

Groups 1 and 2: All rats tolerated the treatment without signs.

Group 3: Bradypnoea, tremor, reduced motility, haircoat ungroomed, piloerection.

Group 4: Bradypnoea, laboured breathing pattern, rales, prostration (lying on side or belly), blepharospasm, mydriasis, chromodacryorrhea, tremor, reduced motility, apathy, haircoat ungroomed, piloerection.

Group 5: Bradypnoea, dyspnoea, laboured breathing pattern, rales, nose/snout area with red encrustations, salivation, blepharospasm, mydriasis, tremor, reduced motility, haircoat ungroomed, piloerection.

Reflex Measurements:

The battery of reflex measurements were made as indicated in the Appendix. Summaries of the reflex data are shown in the Appendix. All animals showed normal reflexes, except some alteration in reflexes in group 4. These changes were consistent with the clinical observations.

Rectal Temperature:

Results of the evaluation of the rectal temperature are summarized in Table 2. Individual data are provided in the Appendix. Statistical comparison between groups exposed to the aerosolized test compound with those in the control group did indicate concentration-dependent effect on body temperature. The changes observed in group 2 are considered to be toxicologically insignificant.

Body Weights:

Individual data as well as evaluations of data concerning body weight gain are included in the Appendix. Statistical comparisons between groups 3 to 5 indicated significantly decreased body weights. Animals of group 2 tolerated the exposure without marked effects on body weights.

Necropsy:

Individual findings from the gross-pathological examinations are shown in the Appendix. A qualitative description, only for findings of toxicological importance and for toxicological evaluation, is given below.

Animals sacrificed at the end of the observation period:

In rats exposed to the test compound a concentration-dependent increased incidence of macroscopical findings could not be observed.

Animals sacrificed during the observation period:

Lung: reddish colour and red foci. Intestine: red mucosa, reddish-slimy content; liver pale and lobulation, renal pelvis: red appearance.

9. EVALUATION AND DISCUSSION

A study on the acute inhalation toxicity of YRC 2894 in rats has been conducted in accordance with OECD Guideline No. 403. The aerosol generated was of adequate respirability in the lower exposure groups (i.e. MMAD ca. 3 μm , GSD ca. 1.7, relative mass < 3 μm ca. 49%). It appeared not feasible to generate concentrations exceeding 500 mg/m³ air using a cyclone. This, in fact, resulted in a decreased respirability of particles. Despite the lower respirability rats died in the higher exposure groups.

Aerosol (dust) concentrations up to and including 481 mg/m³ did not induce test substance related mortality. Exposure to 1523 and 2535 mg/m³ test compound was tolerated without mortality in males but produced mortality in females. Mortality occurred from postexposure day one through seven. Necropsy findings support the conclusion that a causal relationship between lethality and lung damage existed. Exposures to concentrations of 481 mg/m³ and higher were followed by a concentration-dependent signs related to respiratory tract irritation and possibly a nicotinergic like mode of action.

In summary, the aerosolized test substance (dust) proved to have a moderate acute inhalation toxicity to rats. Cumulative evidence suggest that there is a causal relationship of local effects to the respiratory tract and the observed findings.

10. KEY TO ABBREVIATIONS

Konz.	Concentration
nomin.	Nominal
analyt.	Analytical
mcm/ μ m	Micrometer
Expos.	Exposure
MMAD	Mass Median Aerodynamic Diameter
NMAD	Number Median Aerodynamic Diameter
GSD	Geometric standard deviation (GSD)
ECD	Effective cut-off diameter
Ai	Sample for analysis
STAND, S, Std, s	Standard deviation
MW/MEANS	Means
F	F-test value (F-ratio)
DF	Degrees of freedom
PROB	Probability
SS	Total sum of squares
MS	Mean squares
TREATMENT	- between the groups
ERROR	- within the groups
TOTAL	- total
Observation No.: n-nn	Body weight gain from date n to date nn

11. REFERENCES

- ACGIH (American Conference of Governmental Industrial Hygienists) (1978). Air Sampling Instruments for Evaluation of Atmospheric Contaminants, 5th Edition, ACGIH p. F-6. ACGIH section I: Calibration of Air Sampling Instruments and section F: Aerosol Sampling for Particle Size Analysis.
- BCTIC Computer Code Collection - Biomedical computing Technology Information Center, ANOVA a Fortran Program to Perform one-way Classification Analysis of Variance. Vanderbilt Medical Center, Nashville Tennessee, U.S.A.
- BLISS, C.I. (1938). The Determination of the Dosage-Mortality Curve from Small Numbers. Q.J. Pharm. Pharmacol. 11, 192-216.
- CHEMG (1994). Bekanntmachung der Neufassung des Chemikaliengesetzes [Promulgation of the Amended Chemical Law] dated July 25, 1994 Bundesgesetzblatt [federal law gazette] No. 47, date of publication July 29, 1994, Part I, Principles of Good Laboratory Practice.
- DENNIS R.(1976). Handbook of Aerosols - Technical Information Center, Energy Research and Development Administration, S. 110-114, July 1976.
- EG Guideline 86/609/EC (1986). Guideline of the Council dated November 24, 1986 on the Reconciliation of Legal and Administrative Regulations of the Member Countries for the Protection of Animals used for Studies and other Scientific Purposes. Journal of the European Community, Legal Specifications L 358, 29.
- EG Guideline 92/69/EWG. Journal of the European Community - Legal Specifications L 2383 A, 35, December 29, 1992. B.2. Acute Toxicity - Inhalation. p. 121.
- GAD, S.C. and WEIL, C.S. (1982). Statistics for Toxicologists. Principles and Methods of Toxicology, ed. A.W. Hayes, Raven Press, New York, p. 280.
- GREENSPAN, L. (1977). Humidity Fixed Points of Binary Saturated Aqueous Solutions, Journal of Research of the National Bureau of Standards, Vol. 81 A, no. 1, Jan.-Febr. 1977.
- IRWIN, S. (1968). Comprehensive Observational Assessment: Ia: A Systematic, Quantitative Procedure for Assessing the Behavioral and Physiologic State of the Mouse. Psychopharmacologica 13, pp. 222-257.
- MARPLE, V.A. and RUBOW, K.L. (1980). Aerosol Generation Concepts and Parameters in Generation of Aerosols and Facilities for Exposure Experiments, Ed. K. Willeke, Ann Arbor Science Publ. Inc. Mich., pp. 3-29.
- McFARLAND, H.N. (1976). Respiratory Toxicology - Essays in Toxicology, Vol. 7, pp. 121-154, Academic Press Inc., New York, San Francisco, London.
- MOSER, V.C., McCORMIC, J.P., CREASON, J.P., and MacPHAIL, R.C. (1988). Comparison of Chlordimeform and Carbaryl Using a Functional Observational Battery. Fundamental and Applied Toxicology, 11, 189-206.

- OECD - GLP (1983). Publication of the German version of the OECD Principles of Good Laboratory Practice (GLP), *Bundesanzeiger*, 35, No. 42a dated March 2, 1983.
- OECD-Guideline for Testing of Chemicals No. 403. "Acute Inhalation Toxicity", adopted May 12 (1981).
- PAULUHN, J. (1986). Study to Determine Temperature and Humidity Data in Inhalation Chambers; BAYER AG Report No. 15007 dated August 22.
- PAULUHN, J. (1983). Computer-Aided Estimation of the LD₅₀/LC₅₀ BAYER AG Report No. 11835, dated May 18.
- PAULUHN, J. (1994). Validation of an improved nose-only exposure system for rodents. *Journal of Applied Toxicology*, 14:55-62.
- PAULUHN, J. (1988). Different Methods used in Acute and Subchronic Inhalation Studies of Potential Lung Irritants with Particular Attention to Lung Function Measurements. In U. Mohr (ed.), *Inhalation Toxicology - The Design and Interpretation of Inhalation Studies and their Use in Risk Assessment*. Springer Verlag, pp. 87-101.
- PAULUHN, J. (1984). Head-only and nose-only exposure in P. Grosdanoff, R. Baß, U. Hackenberg, D. Henschler, D. Müller, H.-J. Klimisch (eds.), *Problems of Inhalatory Toxicity Studies*, BGA-Schriften, MMV Medizin Verlag München, Vol. 5, pp. 59-68.
- RAABE, O.G. (1982). Deposition and Clearance of Inhaled Aerosols in H. Witschi and P. Nettesheim - Mechanisms in Respiratory Toxicology Vol. I, pp. 27-76, CRC Press, Inc. Boca Raton, Florida.
- ROSIELLO, A.P., ESSIGMANN, J.M., and WOGAN, G.N. (1977). Rapid and Accurate Determination of the Median Lethal Dose (LD₅₀) and its Error with Small Computer. *J. Tox. and Environ. Health* 3, pp. 797-809.
- SNIPES, M.B. (1989). Long-Term Retention and Clearance of Particles Inhaled by Mammalian Species. *Critical Reviews in Toxicology*, Vol. 20, pp. 175-211.
- SOT-COMMENTARY (1992). Recommendations for the Conduct of Acute Inhalation Limit Tests, prepared by the Technical Committee of the Inhalation Specialty Section, Society of Toxicology. *Fundam. Appl. Toxicol.* 18, pp. 321-327.
- TILLERY, M.I., WOOD, G.O., and ETTINGER, J.J. (1976). Generation and Characterization of Aerosols and Vapors for Inhalation Experiments. *Environmental Health Perspectives* 16, pp. 25-40.
- U.S. Environmental Protection Agency (1984). Pesticide assessment guidelines, subdivision F, hazard evaluation: Human and domestic animals (Revised) § 81-3 Acute Inhalation Toxicity Study. NTIS Report PB86-108958, Washington, DC.
- U.S. Environmental Protection Agency 40 CFR Part 160. Federal Insecticide, Fungicide and Rodenticide Act (FIFRA); Good Laboratory Practice Standards (Final Rule); Thursday August 17, 1989.
- U.S. Environmental Protection Agency (1988). Hazard evaluation division: Standard evaluation procedure, inhalation toxicity testing, NTIS Report PB89-100366, Washington, DC.

U.S. Environmental Protection Agency 40 CFR Part 160. Federal Insecticide, Fungicide and Rodenticide Act (FIFRA); Good Laboratory Practice Standards (Final Rule); Thursday August 17, 1989.

U.S. Environmental Protection Agency (1988). Hazard evaluation division: Standard evaluation procedure, inhalation toxicity testing, NTIS Report PB89-100366, Washington, DC.

12. APPENDIX

Atmosphere Characterization

Group	Date of exposure (DD.MM.YY)	Sampled Volume (l) ¹ / flow rate (l/min) ¹	Actual Test Substance Concentrations (mg/m ³ air)	Mean Concentration (mg/m ³ air)
1	12.10.1994	n.a.	0 (air control)	n.a.
2	29.09.1994	20 / 4	85 - 90 - 70 - 75	80
3	23.09.1994	20 / 4	460 - 495 - 480 - 490	481
4	21.09.1994	10 / 4	1530-1570-1280-1710	1523
5	26.09.1994	10 / 4	2440 - 2300 - 2620 - 2780	2535

1) If different volumes or flow rates are used only the maximum value is presented

Characterization of Particle Size Distribution

80 mg/m³ air

Notice: Concentrations reflect design concentrations

ANALYSIS OF PARTICLE DISTRIBUTIONS

Type of investigation: Acute Inhalation - Dust

Compound: YRC 2894

Date of exposure: 29.09.94
Concentration:

Study-no.: T5058291
75.0 mg/m³ air

:	N	Impactor stage (μm - μm)	Cut-Off diameter (μm)	Mass/ stage (mg)	Rel. mass (%)	Cumul. mass (%)	:
:	1	0.06 - 0.12	0.06	.001	.07	.00	:
:	2	0.12 - 0.25	0.12	.003	.21	.07	:
:	3	0.25 - 0.49	0.25	.009	.63	.28	:
:	4	0.49 - 0.90	0.49	.013	.91	.91	:
:	5	0.90 - 1.85	0.90	.145	10.18	1.83	:
:	6	1.85 - 3.69	1.85	.537	37.71	12.01	:
:	7	3.69 - 7.42	3.69	.686	48.17	49.72	:
:	8	7.42 - 14.8	7.42	.030	2.11	97.89	:
:	9	14.8 - 30.	14.8	.000	.00	100.00	:

Mass Median Aerodynamic Diameter (MMAD): 3.05 μm
Geometric standard deviation: 1.67

Number Median Aerodynamic Diameter (NMAD): 1.37 μm
Surface Median Aerodynamic Diameter (SMAD): 2.33 μm

System: BERNER-IMPACTOR I
Air flow: 5.78 liter/min.
Sampling time: 180.00 seconds
Concentration (computed): 82.1 mg per m³ air

Respirability (% < 3 μm):

1. Mass related: 49 % (measured)
2. Number related: 94 % (extrapolated)

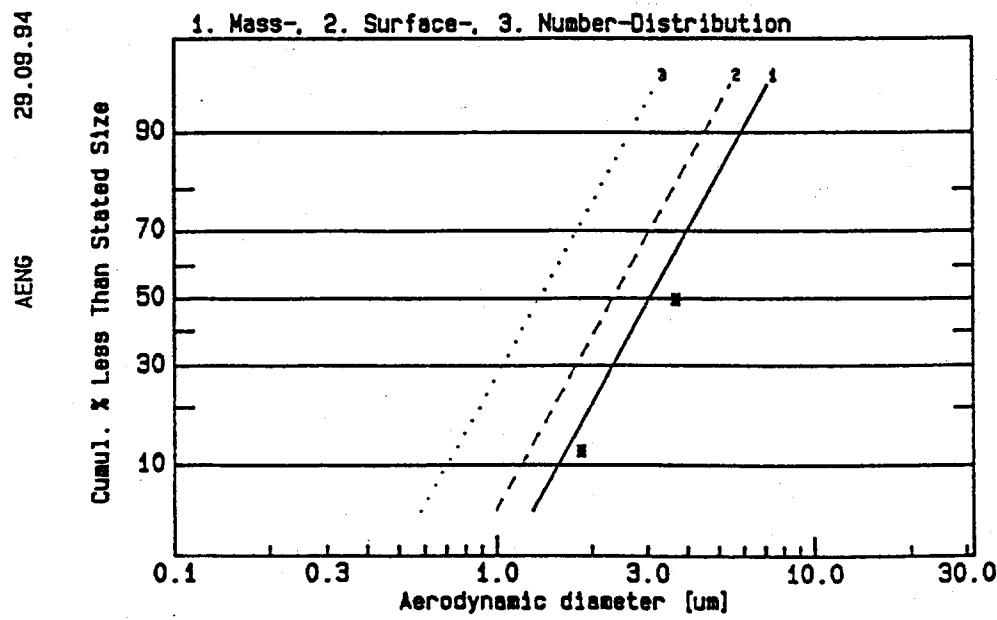
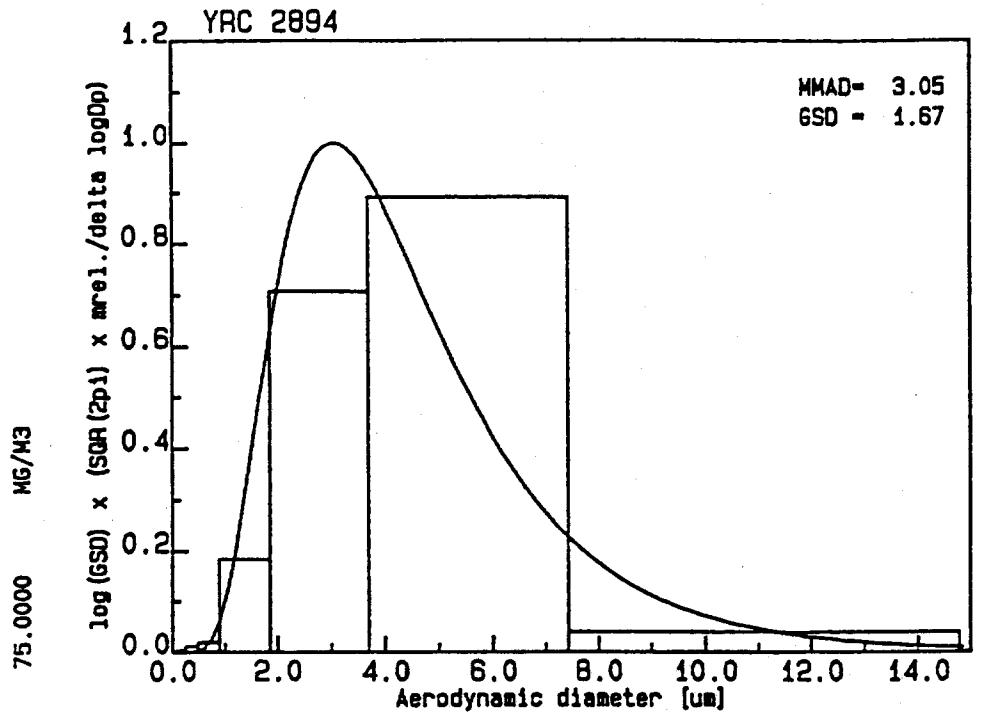
EFFECTIVE CUT-OFF DIAMETER (ECD): The calculation of the cumulative distribution is based on the 'Effective Cut-Off Diameter'.

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Acute Inhalation - Dust

St.-no.: T5058291



Characterization of Particle Size Distribution
481 mg/m³ air

ANALYSIS OF PARTICLE DISTRIBUTIONS

Type of investigation: Acute Inhalation - Dust

Compound: YRC 2894

Date of exposure: 23.09.94
Concentration:

Study-no.: t5058291
500.0 mg/m³ air

:	N	Impactor stage	Cut-Off diameter (μm - μm)	Mass/ stage (mg)	Rel. mass (%)	Cumul. mass (%)	:
:	1	0.06 - 0.12	0.06	.000	.00	.00	:
:	2	0.12 - 0.25	0.12	.001	.05	.00	:
:	3	0.25 - 0.49	0.25	.004	.22	.05	:
:	4	0.49 - 0.90	0.49	.025	1.36	.27	:
:	5	0.90 - 1.85	0.90	.189	10.31	1.64	:
:	6	1.85 - 3.69	1.85	.738	40.24	11.94	:
:	7	3.69 - 7.42	3.69	.826	45.04	52.18	:
:	8	7.42 - 14.8	7.42	.051	2.78	97.22	:
:	9	14.8 - 30.	14.8	.000	.00	100.00	:

Mass Median Aerodynamic Diameter (MMAD): 3.10 μm
Geometric standard deviation: 1.68

Number Median Aerodynamic Diameter (NMAD): 1.36 μm
Surface Median Aerodynamic Diameter (SMAD): 2.36 μm

System: BERNER-IMPACTOR I
Air flow: 5.78 liter/min.
Sampling time: 45.00 seconds
Concentration (computed): 423.1 mg per m³ air

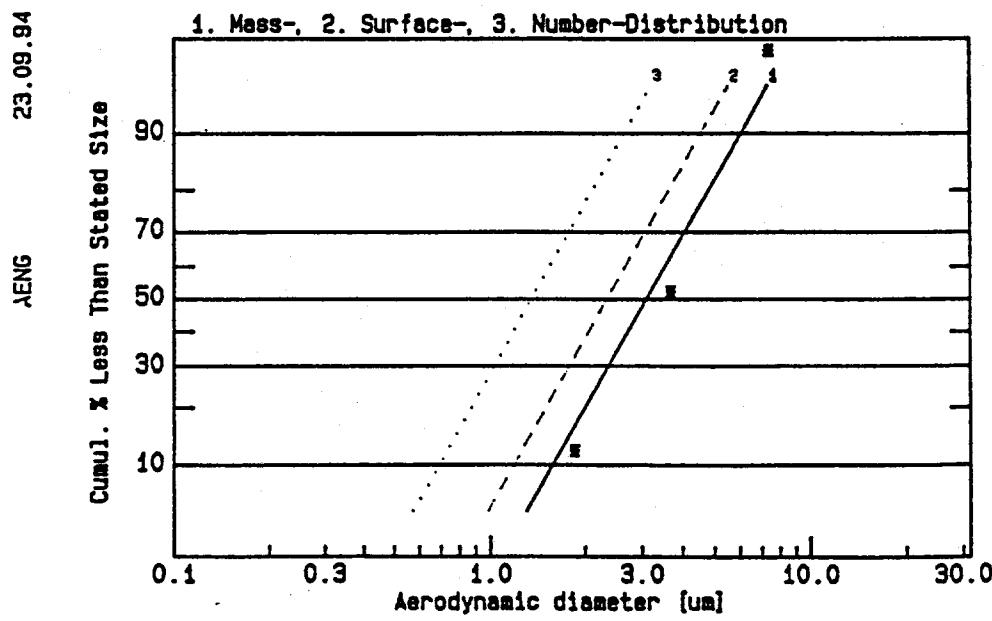
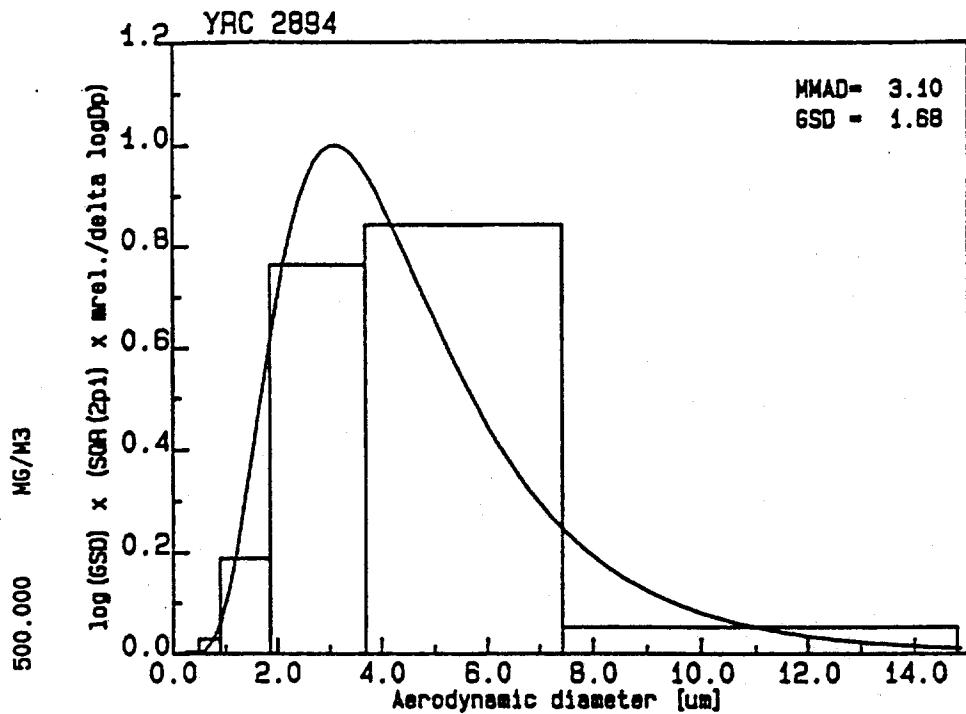
Respirability (% ≤ 3 μm):

1. Mass related: 48 % (measured)
2. Number related: 94 % (extrapolated)

EFFECTIVE CUT-OFF DIAMETER (ECD): The calculation of the cumulative distribution is based on the 'Effective Cut-Off Diameter'.

Acute Inhalation - Dust

St.-no.: t5058291



Characterization of Particle Size Distribution
1523 mg/m³ air

ANALYSIS OF PARTICLE DISTRIBUTIONS

Type of investigation: Acute Inhalation - Dust

Compound: YRC 2894

Date of exposure: 21.09.94 Study-no.: T5058291
Concentration: 1500.0 mg/m³ air

:	N	Impactor stage	Cut-Off diameter (μm - μm)	Mass/ stage (mg)	Rel. mass (%)	Cumul. mass (%)	:
:	1	0.016 - 0.031	0.016	.000	.00	.00	:
:	2	0.031 - 0.063	0.031	.002	.25	.00	:
:	3	0.063 - 0.125	0.063	.004	.51	.25	:
:	4	0.125 - 0.250	0.125	.009	1.14	.76	:
:	5	0.250 - 0.500	0.250	.008	1.01	1.90	:
:	6	0.500 - 1.00	0.500	.012	1.52	2.92	:
:	7	1.00 - 2.00	1.00	.032	4.06	4.44	:
:	8	2.00 - 4.00	2.00	.208	26.36	8.49	:
:	9	4.00 - 8.00	4.00	.339	42.97	34.85	:
:	10	8.00 - 16.0	8.00	.175	22.18	77.82	:
:	11	16.0 - 30.0	16.0	.000	.00	100.00	:

Mass Median Aerodynamic Diameter (MMAD): 5.82 μm
Geometric standard deviation: 3.54

Number Median Aerodynamic Diameter (NMAD): .047 μm
Surface Median Aerodynamic Diameter (SMAD): 1.171 μm

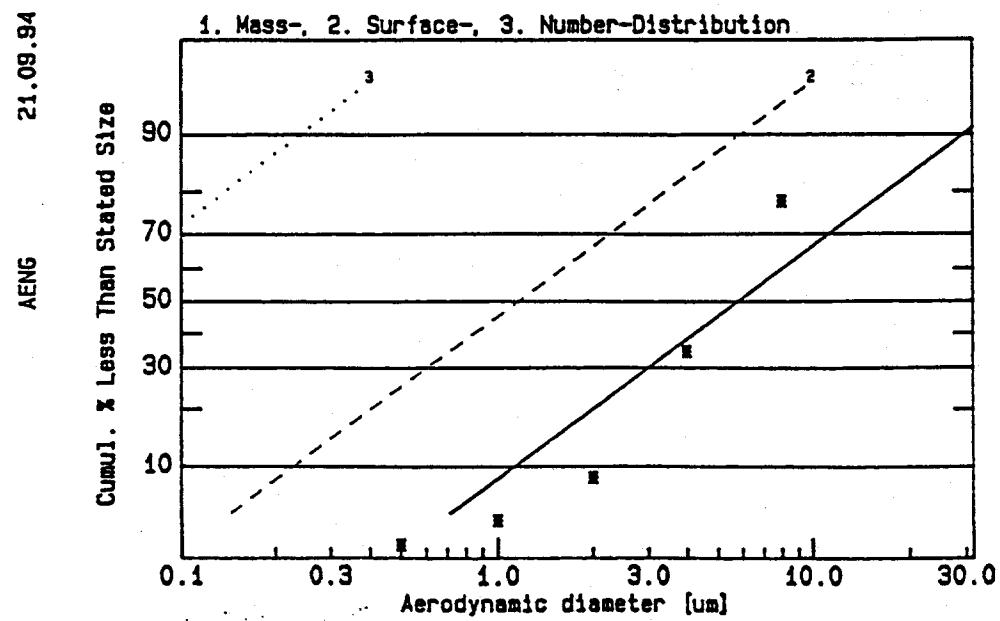
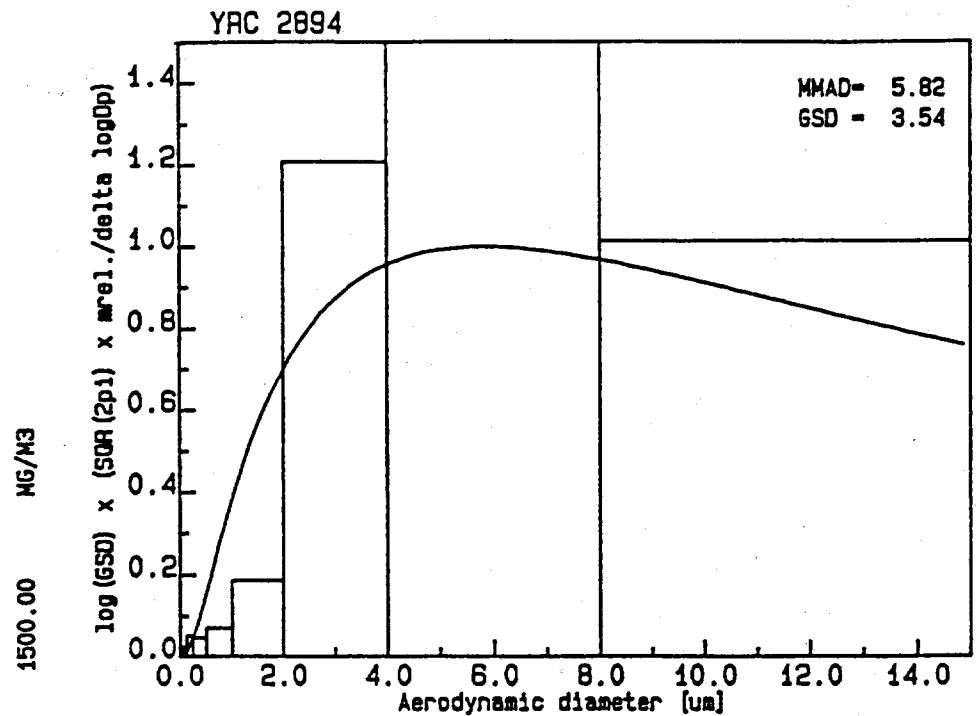
System: BERNER-IMPACTOR II
Air flow: 4.68 liter/min.
Sampling time: 10.00 seconds
Concentration (computed): 1011.5 mg per m³ air

Respirability (% ≤ 3 μm):
1. Mass related: 31 % (measured)
2. Number related: 100 % (extrapolated)

EFFECTIVE CUT-OFF DIAMETER (ECD): The calculation of the cumulative distribution is based on the 'Effective Cut-Off Diameter'.

Acute Inhalation - Dust

St.-no.: T5058291



Characterization of Particle Size Distribution
2535 mg/m³ air

ANALYSIS OF PARTICLE DISTRIBUTIONS

Type of investigation: Acute Inhalation - Dust

Compound: YRC 2894

Date of exposure: 26.09.94

Study-no.: T5058291

Concentration:

2500.0 mg/m³ air

N	Impactor stage	Cut-Off diameter (µm - µm)	Mass/ stage (mg)	Rel. mass (%)	Cumul. mass (%)
1	0.01	0.4	.300	.62	.00
2	0.4	0.7	.100	.21	.62
3	0.7	1.1	.300	.62	.82
4	1.1	2.1	.600	1.23	1.44
5	2.1	3.3	2.100	4.31	2.67
6	3.3	4.7	7.900	16.22	6.98
7	4.7	5.8	4.700	9.65	23.20
8	5.8	9.0	10.700	21.97	32.85
9	9.0	20.0	22.000	45.17	54.83

Mass Median Aerodynamic Diameter (MMAD): 9.10 µm
Geometric standard deviation: 2.35

Number Median Aerodynamic Diameter (NMAD): 1.01 µm
Surface Median Aerodynamic Diameter (SMAD): 4.38 µm

System: ANDERSEN-IMPACTOR

Air flow: 4.00 liter/min.
Sampling time: 300.00 seconds
Concentration (computed): 2435.0 mg per m³ air

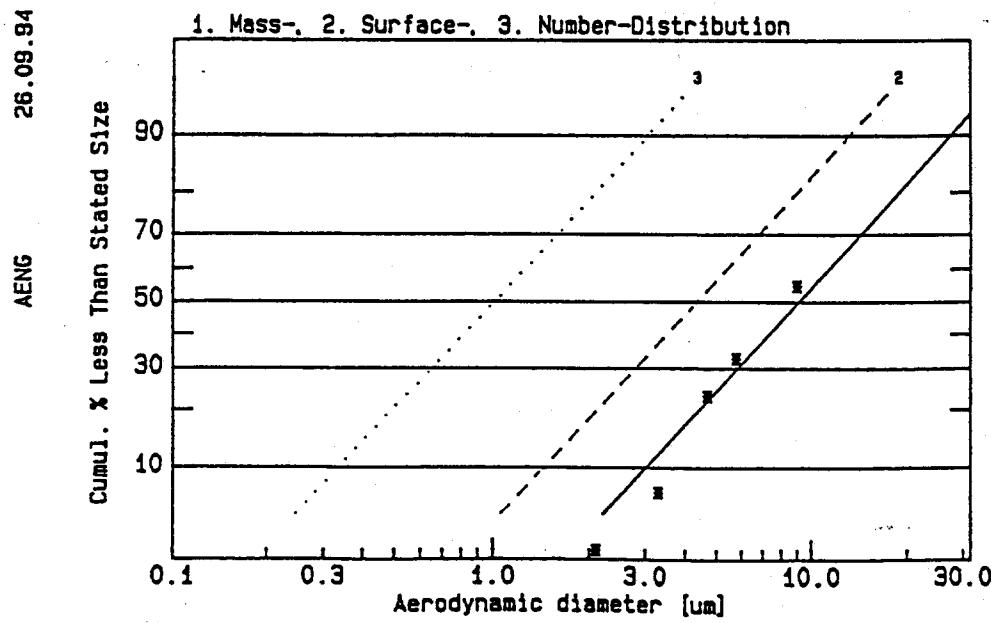
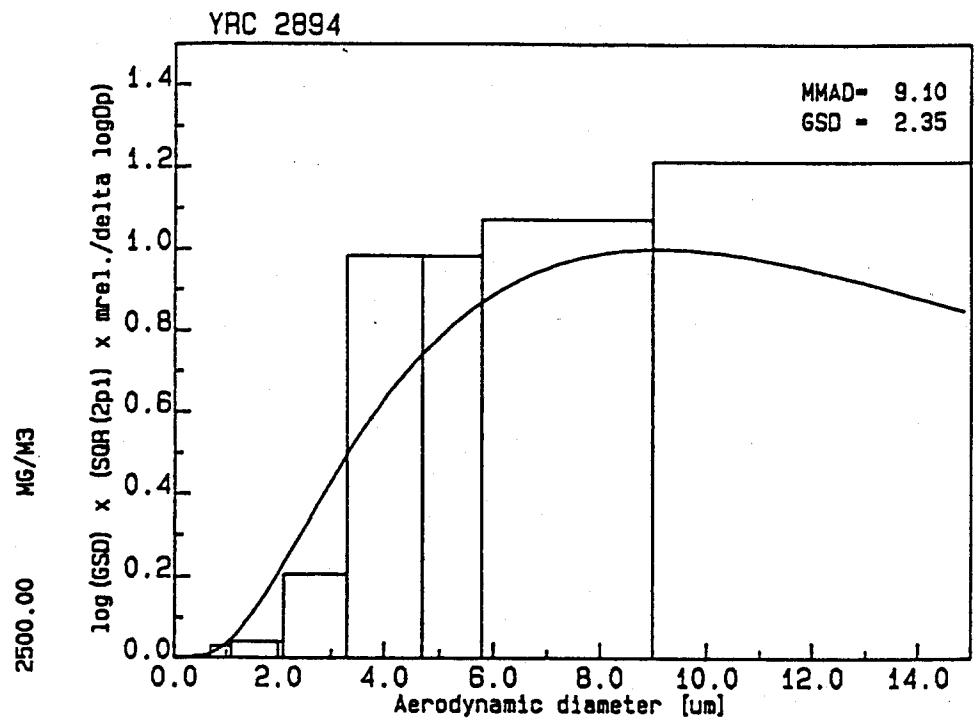
Respirability (% ≤ 3 µm):

1. Mass related: 10 % (measured)
2. Number related: 90 % (extrapolated)

EFFECTIVE CUT-OFF DIAMETER (ECD): The calculation of the cumulative distribution is based on the 'Effective Cut-Off Diameter'.

Acute Inhalation - Dust

St.-no.: T5058291



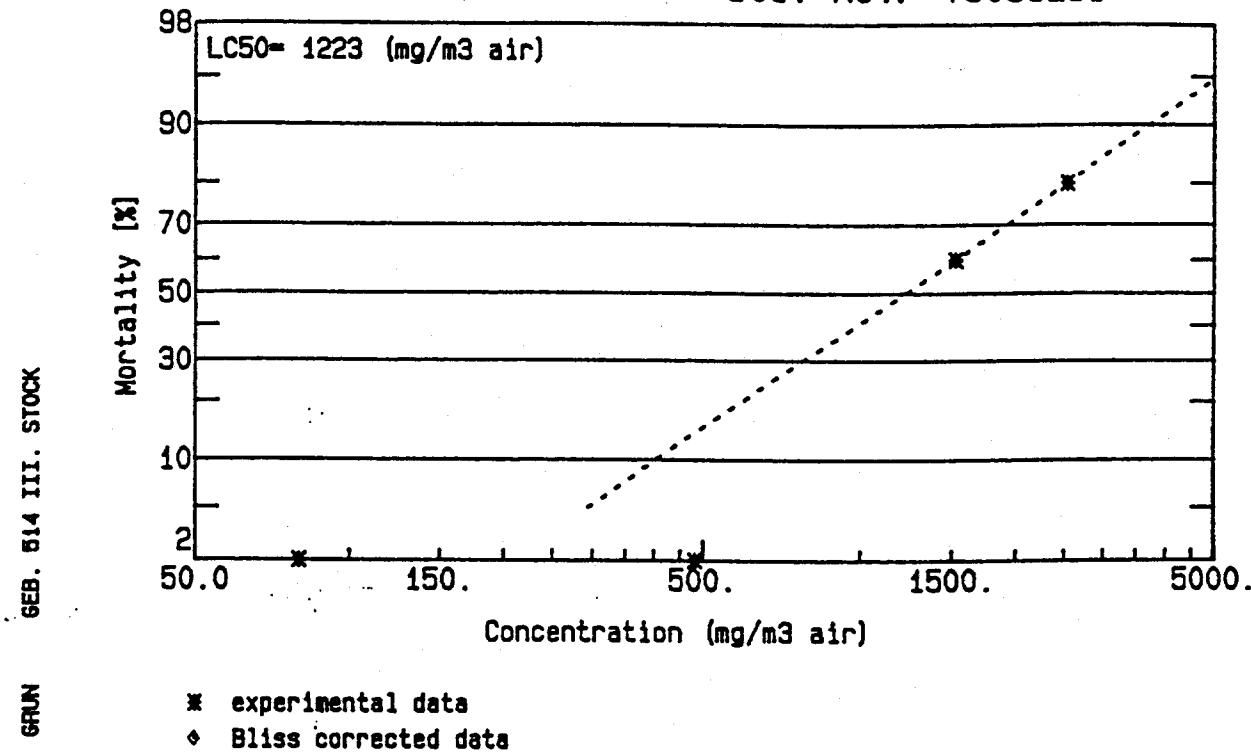
LC50-Calculation

AKUTE INHALATIONSTOXIZITAET

YRC 2894

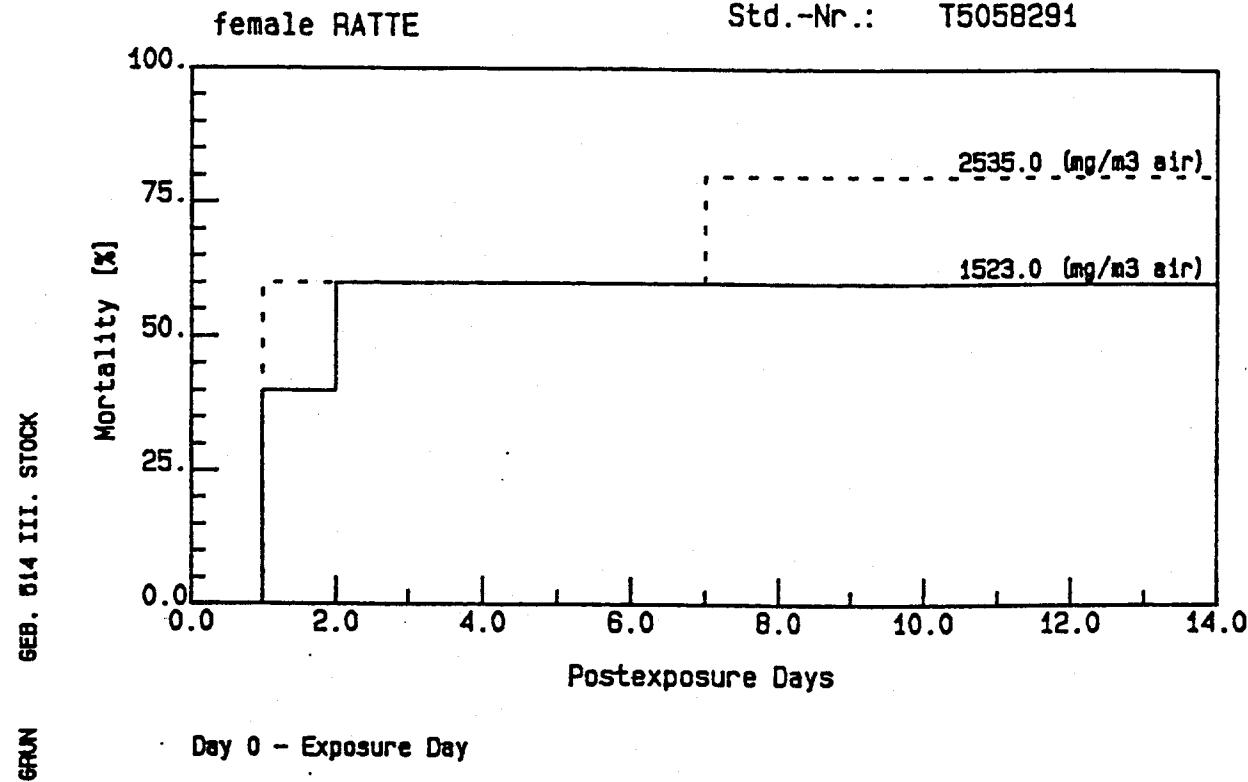
female RATTE

Std.-No.: T5058291



Survival-Curves

AKUTE INHALATIONSTOXIZITAET
YRC 2894



Signs-Incidence-Tables

Test compound: YRC 2894
Study-no: T5058291

Concentration: 0 mg/m³ air / Sex: MALES

Observation	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Bradypnoea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dyspnoea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Labouried breathing pattern	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rales	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lying on belly	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Tremor	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Motility reduced	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lying on side	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Apathy	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Blepharospasm	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mydriasis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Chromodacryorrhea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nose: red encrustations	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Snout/nose area: red encrustat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hair-coat ungroomed	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Surviving animals (N)	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

Legend: n = number of animals with signs

Test compound: YRC 2894
Study-no: T5058291

Concentration: 80 mg/m³ air / sex: MALES

Observation	Day Relative														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Bradypnoea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dyspnoea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Laboured breathing pattern	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rales	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lying on belly	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Tremor	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Motility reduced	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lying on side	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Apathy	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Blepharospasm	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mydriasis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Chromodacryorrhea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nose: red encrustations	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Snout/nose area: red encrustat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hair-coat ungroomed	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Surviving animals (N)	5	5	5	5	5	5	5	5	5	5	5	5	5	5	0

Legend: n = number of animals with signs

Test compound: YRC 2894
Study-no: T5058291

Concentration: 481 mg/m³ air / Sex: MALES

Observation	Day Relative														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Bradypnoea	5	5	2	0	0	0	0	0	0	0	0	0	0	0	0
Dyspnoea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Laboured breathing pattern	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rales	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lying on belly	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Tremor	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Motility reduced	5	5	0	0	0	0	0	0	0	0	0	0	0	0	0
Lying on side	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Apathy	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Blepharospasm	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mydriasis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Chromodacryorrhea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nose: red encrustations	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Snout/nose area: red encrustat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hair-coat ungroomed	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection	3	2	0	0	0	0	0	0	0	0	0	0	0	0	0
Surviving animals (N)	5	5	5	5	5	5	5	5	5	5	5	5	5	5	0

Legend: n = number of animals with signs

Test compound: YRC 2894
study-no: T5058291

Concentration: 1523 mg/m³ air / sex: MALES

Observation	Day Relative														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Bradypnoea	5	5	5	4	2	2	1	0	0	0	0	0	0	0	0
Dyspnoea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Laboured breathing pattern	3	3	2	2	1	0	0	0	0	0	0	0	0	0	0
Rales	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lying on belly	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0
Tremor	4	3	0	0	0	0	0	0	0	0	0	0	0	0	0
Motility reduced	5	5	5	3	2	0	0	0	0	0	0	0	0	0	0
Lying on side	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Apathy	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Blepharospasm	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Mydriasis	4	2	0	0	0	0	0	0	0	0	0	0	0	0	0
Chromodacryorrhea	0	0	2	2	1	0	0	0	0	0	0	0	0	0	0
Nose: red encrustations	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
snout/nose area: red encrustat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
salivation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hair-coat ungroomed	0	0	2	2	0	0	0	0	0	0	0	0	0	0	0
Piloerection	5	5	4	1	1	0	0	0	0	0	0	0	0	0	0
Surviving animals (N)	5	5	5	5	5	5	5	5	5	5	5	5	5	5	0

Legend: n = number of animals with signs

Test compound: YRC 2894
Study-no: T5058291

Concentration: 2535 mg/m³ air / sex: MALES

Observation	Day Relative														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Bradypnoea	5	5	5	5	3	0	0	0	0	0	0	0	0	0	0
Dyspnoea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Laboured breathing pattern	4	3	0	0	0	0	0	0	0	0	0	0	0	0	0
Rales	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lying on belly	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Tremor	5	5	2	1	1	0	0	0	0	0	0	0	0	0	0
Motility reduced	5	5	4	4	0	0	0	0	0	0	0	0	0	0	0
Lying on side	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Apathy	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Blepharospasm	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Mydriasis	5	2	4	2	0	0	0	0	0	0	0	0	0	0	0
Chromodacryorrhea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nose: red encrustations	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Snout/nose area: red encrustat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hair-coat ungroomed	0	3	2	1	0	0	0	0	0	0	0	0	0	0	0
Piloerection	5	5	5	4	0	0	0	0	0	0	0	0	0	0	0
Surviving animals (N)	5	5	5	5	5	5	5	5	5	5	5	5	5	5	0

Legend: n = number of animals with signs

Test compound: YRC 2894
Study-no: T5058291

Concentration: 0 mg/m³ air / Sex: FEMALES

Observation	Day Relative														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Bradypnoea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dyspnoea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Labouring breathing pattern	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rales	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lying on belly	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Tremor	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Motility reduced	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lying on side	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Apathy	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Blepharospasm	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mydriasis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Chromodacryorrhea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nose: red encrustations	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Snout/nose area: red encrustat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hair-coat ungroomed	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Surviving animals (N)	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

Legend: n = number of animals with signs

Test compound: YRC 2894
Study-no: T5058291

Concentration: 80 mg/m³ air / Sex: FEMALES

Observation	Day Relative														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Bradypnoea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dyspnoea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Laboured breathing pattern	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rales	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lying on belly	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Tremor	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Motility reduced	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lying on side	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Apathy	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Blepharospasm	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mydriasis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Chromodacryorrhea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nose: red encrustations	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Snout/nose area: red encrustat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hair-coat ungroomed	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Surviving animals (N)	5	5	5	5	5	5	5	5	5	5	5	5	5	5	0

Legend: n = number of animals with signs

Test compound: YRC 2894
Study-no: T5058291

Concentration: 481 mg/m³ air / Sex: FEMALES

Observation	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Day Relative
Bradypnoea	5	5	3	0	0	0	0	0	0	0	0	0	0	0	0	0
Dyspnoea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Laboured breathing pattern	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rales	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lying on belly	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Tremor	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Motility reduced	5	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Lying on side	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Apathy	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Blepharospasm	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mydriasis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Chromodacryorrhea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nose: red encrustations	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Snout/nose area: red encrustat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hair-coat ungroomed	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Piloerection	3	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Surviving animals (N)	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5

Legend: n = number of animals with signs

Test compound: YRC 2894
study-no: T5058291

Concentration: 1523 mg/m³ air / Sex: FEMALES

Observation	Day Relative														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Bradypnoea	5	3	2	2	1	0	0	0	0	0	0	0	0	0	0
Dyspnoea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Laboured breathing pattern	2	3	0	0	0	0	0	0	0	0	0	0	0	0	0
Rales	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Lying on belly	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Tremor	5	2	0	0	0	0	0	0	0	0	0	0	0	0	0
Motility reduced	5	3	2	2	0	0	0	0	0	0	0	0	0	0	0
Lying on side	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Apathy	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Elepharospasm	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Mydriasis	5	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Chromodacryorrhea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nose: red encrustations	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Snout/nose area: red encrustat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Salivation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hair-coat ungroomed	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0
Piloerection	5	3	2	2	0	0	0	0	0	0	0	0	0	0	0
Surviving animals (N)	5	3	2	2	2	2	2	2	2	2	2	2	2	2	0

Legend: n = number of animals with signs

Test compound: YRC 2894
Study-no: T5058291

Concentration: 2535 mg/m³ air / sex: FEMALES

Observation	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Bradypnoea	5	2	1	1	0	0	0	0	0	0	0	0	0	0	0
Dyspnoea	0	0	1	1	1	1	1	1	0	0	0	0	0	0	0
Labouring breathing pattern	3	2	1	1	0	0	0	0	0	0	0	0	0	0	0
Rales	0	0	1	1	1	1	1	1	0	0	0	0	0	0	0
Lying on belly	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Tremor	4	2	1	1	1	0	0	0	0	0	0	0	0	0	0
Motility reduced	5	2	2	2	2	1	1	1	0	0	0	0	0	0	0
Lying on side	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Apathy	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Blepharospasm	3	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Mydriasis	5	0	1	1	0	0	0	0	0	0	0	0	0	0	0
Chromodacryorrhea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nose: red encrustations	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Snout/nose area: red encrustat	0	1	1	1	1	1	1	1	0	0	0	0	0	0	0
Salivation	0	0	0	1	1	1	1	1	0	0	0	0	0	0	0
Hair-coat ungroomed	0	1	1	1	1	0	0	0	0	0	0	0	0	0	0
piloerection	5	2	2	2	2	1	1	1	0	0	0	0	0	0	0
Surviving animals (N)	5	2	2	2	2	2	2	1	1	1	1	1	1	1	0

Legend: n = number of animals with signs

Test compound: YRC 2894
Study-no: T5050291

Sign: Brachyptosis

Day	Sex	Analytical Concentration - mg/m ³ air											
		0	80	481	1523	2535	0	80	481	1523	2535	F	F
0		0	0	0	0	0	5	2	5	0	0	5	1
1	H	0	0	0	0	0	5	3	2	0	5	3	0
2	H	0	0	0	0	0	5	2	2	1	5	3	0
3	H	0	0	0	0	0	5	0	0	5	0	5	0
4	H	0	0	0	0	0	5	1	1	0	5	0	0
5	H	0	0	0	0	0	5	2	0	0	5	0	0
6	H	0	0	0	0	0	5	0	0	5	0	0	0
7	H	0	0	0	0	0	5	0	0	5	0	0	0
8	H	0	0	0	0	0	5	0	0	5	0	0	0
9	H	0	0	0	0	0	5	0	0	5	0	0	0
10	H	0	0	0	0	0	5	0	0	5	0	0	0
11	H	0	0	0	0	0	5	0	0	5	0	0	0
12	H	0	0	0	0	0	5	0	0	5	0	0	0
13	H	0	0	0	0	0	5	0	0	5	0	0	0
14	H	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, M = males, F = females

Test compound: YRC 2894
Study-no: T5058291

sign: Dyspnoea

Day	Sex	Analytical Concentration - ng/m ³ air														
		0	80	481	1523	2535	0	80	481	1523	2535	0	80	481	1523	2535
	H	I	M	S	N	L	M	S	N	L	M	S	N	L	M	N
0	0	0	0	5	0	0	0	5	0	0	5	0	0	5	0	0
1	0	0	0	5	0	0	0	5	0	0	5	0	0	5	0	0
2	0	0	0	5	0	0	0	5	0	0	5	0	0	5	0	0
3	0	0	0	5	0	0	0	5	0	0	5	0	0	5	0	0
4	0	0	0	5	0	0	0	5	0	0	5	0	0	5	0	0
5	0	0	0	5	0	0	0	5	0	0	5	0	0	5	0	0
6	0	0	0	5	0	0	0	5	0	0	5	0	0	5	0	0
7	0	0	0	5	0	0	0	5	0	0	5	0	0	5	0	0
8	0	0	0	5	0	0	0	5	0	0	5	0	0	5	0	0
9	0	0	0	5	0	0	0	5	0	0	5	0	0	5	0	0
10	0	0	0	5	0	0	0	5	0	0	5	0	0	5	0	0
11	0	0	0	5	0	0	0	5	0	0	5	0	0	5	0	0
12	0	0	0	5	0	0	0	5	0	0	5	0	0	5	0	0
13	0	0	0	5	0	0	0	5	0	0	5	0	0	5	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, H = males, F = females

Test compound: YRC 2894
Study-no: T5058291

Sign: Laboured breathing pattern

Day	Sex	Analytical Concentration - mg/m ³ air											
		0	60	481	1523	2535	0	80	481	1523	2535	F	F
0		0	0	0	0	0	0	0	0	0	0	0	0
1	H	0	0	0	0	0	0	0	0	0	0	0	0
2	H	0	0	0	0	0	0	0	0	0	0	0	0
3	H	0	0	0	0	0	0	0	0	0	0	0	0
4	H	0	0	0	0	0	0	0	0	0	0	0	0
5	H	0	0	0	0	0	0	0	0	0	0	0	0
6	H	0	0	0	0	0	0	0	0	0	0	0	0
7	H	0	0	0	0	0	0	0	0	0	0	0	0
8	H	0	0	0	0	0	0	0	0	0	0	0	0
9	H	0	0	0	0	0	0	0	0	0	0	0	0
10	H	0	0	0	0	0	0	0	0	0	0	0	0
11	H	0	0	0	0	0	0	0	0	0	0	0	0
12	H	0	0	0	0	0	0	0	0	0	0	0	0
13	H	0	0	0	0	0	0	0	0	0	0	0	0
14	H	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, M = males, F = females

Test compound: YRC 2894
Study-no: 15056291

sign: Rates

Day	Sex	Analytical Concentration - ng/m ³ air															
		0	80	481	1523	2535	0	80	481	1523	2535	F	F				
	H	M	H	H	M	N	L	M	S	N	L	M	S	N	L	M	N
0	0	0	5	0	0	5	0	0	5	0	0	5	0	0	5	0	0
1	0	0	5	0	0	5	0	0	5	0	0	5	0	0	5	0	1
2	0	0	5	0	0	5	0	0	5	0	0	5	0	0	5	0	0
3	0	0	5	0	0	5	0	0	5	0	0	5	0	0	5	0	0
4	0	0	5	0	0	5	0	0	5	0	0	5	0	0	5	0	0
5	0	0	5	0	0	5	0	0	5	0	0	5	0	0	5	0	0
6	0	0	5	0	0	5	0	0	5	0	0	5	0	0	5	0	0
7	0	0	5	0	0	5	0	0	5	0	0	5	0	0	5	0	0
8	0	0	5	0	0	5	0	0	5	0	0	5	0	0	5	0	0
9	0	0	5	0	0	5	0	0	5	0	0	5	0	0	5	0	0
10	0	0	5	0	0	5	0	0	5	0	0	5	0	0	5	0	0
11	0	0	5	0	0	5	0	0	5	0	0	5	0	0	5	0	0
12	0	0	5	0	0	5	0	0	5	0	0	5	0	0	5	0	0
13	0	0	5	0	0	5	0	0	5	0	0	5	0	0	5	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, H = males, F = females

Test compound: VRC 2894
Study-no: 15058291

Sign: Lying on belly

Day	Sex	Analytical Concentration - mg/m ³ air											
		0	60	481	1523	2335	0	80	481	1523	2335	F	F
0		0	0	0	0	0	0	0	0	0	0	0	0
1	H	0	0	0	0	0	0	0	0	0	0	0	0
2	H	0	0	0	0	0	0	0	0	0	0	0	0
3	H	0	0	0	0	0	0	0	0	0	0	0	0
4	H	0	0	0	0	0	0	0	0	0	0	0	0
5	H	0	0	0	0	0	0	0	0	0	0	0	0
6	H	0	0	0	0	0	0	0	0	0	0	0	0
7	H	0	0	0	0	0	0	0	0	0	0	0	0
8	H	0	0	0	0	0	0	0	0	0	0	0	0
9	H	0	0	0	0	0	0	0	0	0	0	0	0
10	H	0	0	0	0	0	0	0	0	0	0	0	0
11	H	0	0	0	0	0	0	0	0	0	0	0	0
12	H	0	0	0	0	0	0	0	0	0	0	0	0
13	H	0	0	0	0	0	0	0	0	0	0	0	0
14	H	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, H = males, F = females

Test compound: YRC 2894
Study no: 15056291

Sign: Tremor

Day	Sex	Analytical Concentration - mg/m ³ air														
		0	80	481	1523	2535	0	80	481	1523	2535	0	80	481	1523	2535
	H	H	H	H	H	H	F	F	F	F	F	F	F	F	F	F
0	0	0	0	5	0	0	5	2	0	0	5	0	0	5	1	0
1	0	0	0	5	0	0	5	0	0	5	4	1	0	5	0	2
2	0	0	0	5	0	0	5	0	0	5	2	0	5	0	0	3
3	0	0	0	5	0	0	5	0	0	5	1	0	5	0	0	2
4	0	0	0	5	0	0	5	0	0	5	1	0	5	0	0	2
5	0	0	0	5	0	0	5	0	0	5	0	0	5	0	0	2
6	0	0	0	5	0	0	5	0	0	5	0	0	5	0	0	2
7	0	0	0	5	0	0	5	0	0	5	0	0	5	0	0	2
8	0	0	0	5	0	0	5	0	0	5	0	0	5	0	0	1
9	0	0	0	5	0	0	5	0	0	5	0	0	5	0	0	1
10	0	0	0	5	0	0	5	0	0	5	0	0	5	0	0	1
11	0	0	0	5	0	0	5	0	0	5	0	0	5	0	0	1
12	0	0	0	5	0	0	5	0	0	5	0	0	5	0	0	1
13	0	0	0	5	0	0	5	0	0	5	0	0	5	0	0	1
14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, M = males, F = females

Test compound: YRC 2894
Study-no: T30508291

Sign: Motility reduced

Day	Sex	Analytical Concentration - mg/m ³ air											
		0	80	481	1523	2535	0	80	481	1523	2535	F	F
	I	M	S	N	L	M	S	N	L	M	S	N	L
0	0	0	0	5	0	0	5	3	2	0	5	4	0
1	0	0	0	5	0	0	5	4	1	0	5	0	0
2	0	0	0	5	0	0	5	0	2	0	5	0	0
3	0	0	0	5	0	0	5	0	0	5	0	0	0
4	0	0	0	5	0	0	5	0	1	0	5	0	0
5	0	0	0	5	0	0	5	0	0	5	0	0	0
6	0	0	0	5	0	0	5	0	0	5	0	0	0
7	0	0	0	5	0	0	5	0	0	5	0	0	0
8	0	0	0	5	0	0	5	0	0	5	0	0	0
9	0	0	0	5	0	0	5	0	0	5	0	0	0
10	0	0	0	5	0	0	5	0	0	5	0	0	0
11	0	0	0	5	0	0	5	0	0	5	0	0	0
12	0	0	0	5	0	0	5	0	0	5	0	0	0
13	0	0	0	5	0	0	5	0	0	5	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, M = males, F = females

Test compound: YRC 2894
Study-no: 15058291

sign: lying on side

Day	Sex	Analytical Concentration - mg/m ³ air											
		0	80	481	1523	2535	0	80	481	1523	2535	F	F
0	H	0	0	5	0	0	5	0	0	5	0	0	5
1	H	0	0	5	0	0	5	0	0	5	0	0	5
2	H	0	0	5	0	0	5	0	0	5	0	0	5
3	H	0	0	5	0	0	5	0	0	5	0	0	5
4	H	0	0	5	0	0	5	0	0	5	0	0	5
5	H	0	0	5	0	0	5	0	0	5	0	0	5
6	H	0	0	5	0	0	5	0	0	5	0	0	5
7	H	0	0	5	0	0	5	0	0	5	0	0	5
8	H	0	0	5	0	0	5	0	0	5	0	0	5
9	H	0	0	5	0	0	5	0	0	5	0	0	5
10	H	0	0	5	0	0	5	0	0	5	0	0	5
11	H	0	0	5	0	0	5	0	0	5	0	0	5
12	H	0	0	5	0	0	5	0	0	5	0	0	5
13	H	0	0	5	0	0	5	0	0	5	0	0	5
14	H	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, H = survivors, M = males, F = females

Test compound: YRC 2894
Study-no: TS058291

sign: Apathy

Day	Sex	Analytical Concentration - ng/m ³ air											
		0	80	481	1523	2535	0	80	481	1523	2535	0	F
0		0	0	0	0	0	0	0	0	0	0	0	0
1	H	0	0	0	0	0	0	0	0	0	0	0	0
2	H	0	0	0	0	0	0	0	0	0	0	0	0
3	H	0	0	0	0	0	0	0	0	0	0	0	0
4	H	0	0	0	0	0	0	0	0	0	0	0	0
5	H	0	0	0	0	0	0	0	0	0	0	0	0
6	H	0	0	0	0	0	0	0	0	0	0	0	0
7	H	0	0	0	0	0	0	0	0	0	0	0	0
8	H	0	0	0	0	0	0	0	0	0	0	0	0
9	H	0	0	0	0	0	0	0	0	0	0	0	0
10	H	0	0	0	0	0	0	0	0	0	0	0	0
11	H	0	0	0	0	0	0	0	0	0	0	0	0
12	H	0	0	0	0	0	0	0	0	0	0	0	0
13	H	0	0	0	0	0	0	0	0	0	0	0	0
14	H	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, H = survivors, M = males, F = females

Test compound: YRC 2894
Study no: T5058291

Sign: Blepharospasm

Day	Sex	Analytical Concentration - ng/m ³ air														
		0	80	481	1523	2535	0	80	481	1523	2535	0	80	481	1523	2535
	H	H	H	H	H	F	F	F	F	F	F	F	F	F	F	F
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, M = males, F = females

Test compound: YRC 2894
Study no: T5058291

Sign: Hydnrosis

Day	Sex	Analytical Concentration - mg/m ³ air												
		0	80	481	1523	2535	0	80	481	1523	2535	F	F	N
0	H	0	0	0	0	0	0	0	0	0	0	0	0	0
1	H	0	0	0	0	0	0	0	0	0	0	0	0	0
2	H	0	0	0	0	0	0	0	0	0	0	0	0	0
3	H	0	0	0	0	0	0	0	0	0	0	0	0	0
4	H	0	0	0	0	0	0	0	0	0	0	0	0	0
5	H	0	0	0	0	0	0	0	0	0	0	0	0	0
6	H	0	0	0	0	0	0	0	0	0	0	0	0	0
7	H	0	0	0	0	0	0	0	0	0	0	0	0	0
8	H	0	0	0	0	0	0	0	0	0	0	0	0	0
9	H	0	0	0	0	0	0	0	0	0	0	0	0	0
10	H	0	0	0	0	0	0	0	0	0	0	0	0	0
11	H	0	0	0	0	0	0	0	0	0	0	0	0	0
12	H	0	0	0	0	0	0	0	0	0	0	0	0	0
13	H	0	0	0	0	0	0	0	0	0	0	0	0	0
14	H	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, H = males, F = females

Test compound: YRC 2894
Study-no: T5056291

sign: *carcassdaeryorxha*

Day	Sex	Analytical Concentration - mg/m ³ air											
		0	80	481	1523	2535	0	80	481	1523	F	P	P
	M	M	M	M	N	N	N	N	1 m	s	N	1 m	s
0	0	0	0	5	0	0	0	5	0	0	5	0	0
1	0	0	0	5	0	0	0	5	0	0	5	0	0
2	0	0	0	5	0	0	0	5	0	0	5	0	0
3	0	0	0	5	0	0	0	5	0	0	5	0	0
4	0	0	0	5	0	0	0	5	0	0	5	0	0
5	0	0	0	5	0	0	0	5	0	0	5	0	0
6	0	0	0	5	0	0	0	5	0	0	5	0	0
7	0	0	0	5	0	0	0	5	0	0	5	0	0
8	0	0	0	5	0	0	0	5	0	0	5	0	0
9	0	0	0	5	0	0	0	5	0	0	5	0	0
10	0	0	0	5	0	0	0	5	0	0	5	0	0
11	0	0	0	5	0	0	0	5	0	0	5	0	0
12	0	0	0	5	0	0	0	5	0	0	5	0	0
13	0	0	0	5	0	0	0	5	0	0	5	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: 1 = slight, m = moderate, s = severe, N = survivors, M = males, F = females

Test compound: YRC 2896
Study-no: 15056291

sign: Snout/nose area: red encrustations

Day	Sex	Analytical Concentration - mg/m ³ air														
		0	80	481	1523	2535	0	80	481	1523	2535	0	80	481	1523	2535
0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	H	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	H	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	H	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	H	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	H	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	H	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	H	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8	H	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9	H	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	H	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11	H	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	H	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13	H	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14	H	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, H = males, F = females

Test compound: YRC 2894
Study-no: T5056291

Sign: Salivation

Day	Sex	Analytical Concentration - mg/m ³ air											
		0	80	481	1523	2535	0	80	481	1523	2535	F	F
	H	H	H	H	H	H	H	H	H	H	H	H	H
0	0	0	0	5	0	0	5	0	0	5	0	0	5
1	0	0	0	5	0	0	5	0	0	5	0	0	5
2	0	0	0	5	0	0	5	0	0	5	0	0	5
3	0	0	0	5	0	0	5	0	0	5	0	0	5
4	0	0	0	5	0	0	5	0	0	5	0	0	5
5	0	0	0	5	0	0	5	0	0	5	0	0	5
6	0	0	0	5	0	0	5	0	0	5	0	0	5
7	0	0	0	5	0	0	5	0	0	5	0	0	5
8	0	0	0	5	0	0	5	0	0	5	0	0	5
9	0	0	0	5	0	0	5	0	0	5	0	0	5
10	0	0	0	5	0	0	5	0	0	5	0	0	5
11	0	0	0	5	0	0	5	0	0	5	0	0	5
12	0	0	0	5	0	0	5	0	0	5	0	0	5
13	0	0	0	5	0	0	5	0	0	5	0	0	5
14	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, H = survivors, M = males, F = females

Test compound: YAC 2894
Study-no: 15058291

Sign: Hair-coat ungroomed

Day	Sex	Analytical Concentration - mg/m ³ air													
		0	80	481	1523	2535	0	80	481	1523	2535	F	F	M	N
0	H	0	0	5	0	0	5	0	0	5	0	0	0	5	0
1	H	0	0	5	1	0	0	5	0	0	5	0	0	5	0
2	H	0	0	5	0	0	5	1	0	5	2	0	0	5	0
3	H	0	0	5	0	0	5	1	0	5	1	0	0	5	1
4	H	0	0	5	0	0	5	2	0	5	0	0	0	5	0
5	H	0	0	5	0	0	5	0	0	5	0	0	0	5	0
6	H	0	0	5	0	0	5	0	0	5	0	0	0	5	0
7	H	0	0	5	0	0	5	0	0	5	0	0	0	5	0
8	H	0	0	5	0	0	5	0	0	5	0	0	0	5	0
9	H	0	0	5	0	0	5	0	0	5	0	0	0	5	0
10	H	0	0	5	0	0	5	0	0	5	0	0	0	5	0
11	H	0	0	5	0	0	5	0	0	5	0	0	0	5	0
12	H	0	0	5	0	0	5	0	0	5	0	0	0	5	0
13	H	0	0	5	0	0	5	0	0	5	0	0	0	5	0
14	H	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, H = males, F = females

Test compound: YRC 2894
Study-no: T5058291

sign: filterrection

Sex	Day	Analytical Concentration - mg/m ³ air													
		0	80	481	1523	2535	0	80	481	1523	2535	F	F	F	F
L	m	s	N	l	m	s	N	l	m	s	N	l	m	N	l
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Legend: l = slight, m = moderate, s = severe, N = survivors, M = males, F = females

Test compound: YRC 2894
Study-no: T5058291

Sign: Bradypnoea

Day	Sex	Analytical Concentration - mg/m ³ air									
		0		80		481		1523		2535	
		M	M	M	M	M	M	F	F	F	F
0		0/ 5	0/ 5	5/ 5	5/ 5	5/ 5	5/ 5	0/ 5	0/ 5	5/ 5	5/ 5
1		0/ 5	0/ 5	5/ 5	5/ 5	5/ 5	5/ 5	0/ 5	0/ 5	5/ 5	3/ 3
2		0/ 5	0/ 5	2/ 5	5/ 5	5/ 5	5/ 5	0/ 5	0/ 5	3/ 5	2/ 2
3		0/ 5	0/ 5	0/ 5	4/ 5	5/ 5	5/ 5	0/ 5	0/ 5	0/ 5	2/ 2
4		0/ 5	0/ 5	0/ 5	2/ 5	3/ 5	3/ 5	0/ 5	0/ 5	0/ 5	1/ 2
5		0/ 5	0/ 5	0/ 5	2/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2
6		0/ 5	0/ 5	0/ 5	1/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2
7		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
8		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
9		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
10		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
11		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
12		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
13		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
14		0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0

Legend: n = number of animals with signs, N = survivors
M = males, F = females

Test compound: YRC 2894
Study-no: T5058291

Sign: Dyspnoea

Sex	Analytical Concentration - mg/m ³ air									
	0	80	481	1523	2535	0	80	481	1523	2535
Day	M n/N	M n/N	M n/N	M n/N	M n/N	F n/N	F n/N	F n/N	F n/N	F n/N
0	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5
1	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2
2	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2
3	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2
4	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2
5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2
6	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2
7	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
8	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
9	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
10	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
11	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
12	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
13	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
14	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0

Legend: n = number of animals with signs, N = survivors
M = males, F = females

Test compound: YRC 2894

Study-no: T5058291

Sign: Laboured breathing pattern

Sex Day	Analytical Concentration - mg/m ³ air											
	0		80		481		1523		2535		0	
	M n/N	M n/N	M n/N	M n/N	M n/N	M n/N	F n/N	F n/N	F n/N	F n/N	F n/N	F n/N
0	0/ 5	0/ 5	0/ 5	0/ 5	3/ 5	4/ 5	0/ 5	0/ 5	0/ 5	0/ 5	2/ 5	3/ 5
1	0/ 5	0/ 5	0/ 5	0/ 5	3/ 5	3/ 5	0/ 5	0/ 5	0/ 5	0/ 5	3/ 3	2/ 2
2	0/ 5	0/ 5	0/ 5	0/ 5	2/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2
3	0/ 5	0/ 5	0/ 5	0/ 5	2/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2
4	0/ 5	0/ 5	0/ 5	0/ 5	1/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
6	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
7	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
8	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
9	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
10	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
11	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
12	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
13	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
14	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0

Legend: n = number of animals with signs, N = survivors
M = males, F = females

Test compound: YRC 2894

Study-no: T5058291

Sign: Rales

Sex Day	Analytical Concentration - mg/m ³ air									
	0 M n/N	80 M n/N	481 M n/N	1523 M n/N	2535 M n/N	0 F n/N	80 F n/N	481 F n/N	1523 F n/N	2535 F n/N
0	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5
1	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2
2	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2
3	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2
4	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2
5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2
6	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2
7	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
8	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
9	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
10	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
11	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
12	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
13	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
14	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0

Legend: n = number of animals with signs, N = survivors
M = males, F = females

Test compound: YRC 2894

Study-no: T5058291

Sign: Lying on belly

Sex Day	Analytical Concentration - mg/m ³ air									
	0		80		481		1523		2535	
	M n/N	M n/N	M n/N	M n/N	M n/N	F n/N	F n/N	F n/N	F n/N	F n/N
0	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5
1	0/ 5	0/ 5	0/ 5	2/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	1/ 3
2	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2
3	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2
4	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2
5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2
6	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2
7	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
8	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
9	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
10	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
11	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
12	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
13	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
14	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0

Legend: n = number of animals with signs, N = survivors

M = males, F = females

Test compound: YRC 2894
Study-no: T5058291

Sign: Tremor

Sex	Analytical Concentration - mg/m ³ air											
	0			80			481			1523		
	M	M	M	M	M	M	F	F	F	F	F	F
Day	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N
0	0/ 5	0/ 5	2/ 5	4/ 5	5/ 5	0/ 5	0/ 5	1/ 5	5/ 5	4/ 5		
1	0/ 5	0/ 5	0/ 5	3/ 5	5/ 5	0/ 5	0/ 5	0/ 5	0/ 5	2/ 3	2/ 2	
2	0/ 5	0/ 5	0/ 5	0/ 5	2/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2	
3	0/ 5	0/ 5	0/ 5	0/ 5	1/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2	
4	0/ 5	0/ 5	0/ 5	0/ 5	1/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2	
5	0/ 5	0/ 5	0/ 5	0/ 5	1/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2	
6	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2	
7	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2	
8	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1	
9	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1	
10	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1	
11	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1	
12	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1	
13	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1	
14	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	

Legend: n = number of animals with signs, N = survivors
M = males, F = females

Test compound: YRC 2894

Study-no: T5058291

Sign: Motility reduced

Sex	Analytical Concentration - mg/m ³ air											
	0			80			481			1523		
	M	M	M	M	M	M	F	F	F	F	F	F
Day	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N
0	0/ 5	0/ 5	5/ 5	5/ 5	5/ 5	5/ 5	0/ 5	0/ 5	5/ 5	5/ 5	5/ 5	5/ 5
1	0/ 5	0/ 5	5/ 5	5/ 5	5/ 5	5/ 5	0/ 5	0/ 5	5/ 5	5/ 5	3/ 3	2/ 2
2	0/ 5	0/ 5	0/ 5	5/ 5	5/ 5	4/ 5	0/ 5	0/ 5	0/ 5	0/ 5	2/ 2	2/ 2
3	0/ 5	0/ 5	0/ 5	3/ 5	4/ 5	0/ 5	0/ 5	0/ 5	0/ 5	2/ 2	2/ 2	2/ 2
4	0/ 5	0/ 5	0/ 5	2/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	2/ 2
5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2
6	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2
7	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
8	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
9	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
10	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
11	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
12	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
13	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
14	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0

Legend: n = number of animals with signs, N = survivors
M = males, F = females

Test compound: YRC 2894

Study-no: T5058291

Sign: Lying on side

Sex Day	Analytical Concentration - mg/m ³ air									
	0 n/N	80 n/N	481 n/N	1523 n/N	2535 n/N	0 n/N	80 n/N	481 n/N	1523 n/N	2535 n/N
	M	M	M	M	M	F	F	F	F	F
0	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5
1	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	1/ 3	0/ 2
2	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
3	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
4	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
6	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
7	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
8	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
9	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
10	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
11	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
12	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
13	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
14	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0

Legend: n = number of animals with signs, N = survivors
M = males, F = females

Test compound: YRC 2894

Study-no: T5058291

Sign: Apathy

Sex	Analytical Concentration - mg/m ³ air											
	0			80			481			1523		
	M	M	M	M	M	M	F	F	F	F	F	F
Day	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N
0	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5
1	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	1/ 3	0/ 2
2	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
3	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
4	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
6	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
7	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
8	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
9	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
10	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
11	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
12	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
13	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
14	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0

Legend: n = number of animals with signs, N = survivors

M = males, F = females

Test compound: YRC 2894

Study-no: T5058291

Sign: Blepharospasm

Sex Day	Analytical Concentration - mg/m ³ air											
	0		80		481		1523		2535		0	
	M	M	M	M	M	M	F	F	F	F	F	F
	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N
0	0/ 5	0/ 5	0/ 5	0/ 5	1/ 5	1/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	3/ 5
1	0/ 5	0/ 5	0/ 5	0/ 5	1/ 5	1/ 5	0/ 5	0/ 5	0/ 5	0/ 5	1/ 3	1/ 2
2	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
3	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
4	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
6	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
7	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
8	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
9	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
10	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
11	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
12	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
13	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
14	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0

Legend: n = number of animals with signs, N = survivors
M = males, F = females

Test compound: YRC 2894

Study-no: T5058291

Sign: Mydriasis

Sex Day	Analytical Concentration - mg/m ³ air									
	0 n/N	80 n/N	481 n/N	1523 n/N	2535 n/N	0 n/N	80 n/N	481 n/N	1523 n/N	2535 n/N
	M	M	M	M	M	F	F	F	F	F
0	0/ 5	0/ 5	0/ 5	4/ 5	5/ 5	0/ 5	0/ 5	0/ 5	5/ 5	5/ 5
1	0/ 5	0/ 5	0/ 5	2/ 5	2/ 5	0/ 5	0/ 5	0/ 5	1/ 3	0/ 2
2	0/ 5	0/ 5	0/ 5	0/ 5	4/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2
3	0/ 5	0/ 5	0/ 5	0/ 5	2/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2
4	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
6	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
7	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
8	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
9	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
10	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
11	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
12	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
13	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
14	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0

Legend: n = number of animals with signs, N = survivors

M = males, F = females

Test compound: YRC 2894

Study-no: T5058291

Sign: Chromodacryorrhea

Day	Sex	Analytical Concentration - mg/m ³ air									
		0	80	481	1523	2535	0	80	481	1523	2535
		M	M	M	M	M	F	F	F	F	F
n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N
0		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5
1		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 3	0/ 2
2		0/ 5	0/ 5	0/ 5	2/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
3		0/ 5	0/ 5	0/ 5	2/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
4		0/ 5	0/ 5	0/ 5	1/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
5		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
6		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
7		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
8		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
9		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
10		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
11		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
12		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
13		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
14		0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0

Legend: n = number of animals with signs, N = survivors

M = males, F = females

Test compound: YRC 2894

Study-no: T5058291

Sign: Nose: red encrustations

Day	Sex	Analytical Concentration - mg/m ³ air									
		0	80	481	1523	2535	0	80	481	1523	2535
		M	M	M	M	M	F	F	F	F	F
n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N
0		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5
1		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 3	0/ 2
2		0/ 5	0/ 5	0/ 5	0/ 5	1/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
3		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
4		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
5		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
6		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2
7		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
8		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
9		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
10		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
11		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
12		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
13		0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
14		0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0

Legend: n = number of animals with signs, N = survivors
M = males, F = females

Test compound: YRC 2894

Study-no: T5058291

Sign: Snout/nose area: red encrustations

Sex	Analytical Concentration - mg/m ³ air									
	0	80	481	1523	2535	0	80	481	1523	2535
	M	M	M	M	M	F	F	F	F	F
Day	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N	n/N
0	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5
1	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 3
2	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	1/ 2
3	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	1/ 2
4	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	1/ 2
5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	1/ 2
6	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	1/ 2
7	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
8	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
9	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
10	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
11	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
12	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
13	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
14	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0

Legend: n = number of animals with signs, N = survivors

M = males, F = females

Test compound: YRC 2894

Study-no: T5058291

Sign: Salivation

Sex Day	Analytical Concentration - mg/m ³ air											
	O M n/N	80 M n/N	481 M n/N	1523 M n/N	2535 M n/N	O F n/N	80 F n/N	481 F n/N	1523 F n/N	2535 F n/N	0	
	0	80	481	1523	2535	0	80	481	1523	2535	0	
0	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	
1	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 3	0/ 2	
2	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 2	
3	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2	
4	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2	
5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2	
6	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2	
7	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1	
8	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1	
9	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1	
10	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1	
11	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1	
12	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1	
13	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1	
14	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	

Legend: n = number of animals with signs, N = survivors

M = males, F = females

Test compound: YRC 2894

Study-no: T5058291

Sign: Hair-coat ungroomed

Sex Day	Analytical Concentration - mg/m ³ air									
	0					80				
	M n/N	M n/N	M n/N	M n/N	M n/N	F n/N	F n/N	F n/N	F n/N	F n/N
0	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5
1	0/ 5	0/ 5	1/ 5	0/ 5	3/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 3
2	0/ 5	0/ 5	0/ 5	2/ 5	2/ 5	0/ 5	0/ 5	0/ 5	0/ 5	1/ 2
3	0/ 5	0/ 5	0/ 5	2/ 5	1/ 5	0/ 5	0/ 5	0/ 5	0/ 5	1/ 2
4	0/ 5	0/ 5	0/ 5	2/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	1/ 2
5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2
6	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2
7	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
8	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
9	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
10	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
11	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
12	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
13	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 1
14	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0

Legend: n = number of animals with signs, N = survivors

M = males, F = females

Test compound: YRC 2894

Study-no: T5058291

Sign: Piloerection

Sex Day	Analytical Concentration - mg/m ³ air									
	0		80		481		1523		2535	
	M n/N	M n/N	M n/N	M n/N	M n/N	F n/N	F n/N	F n/N	F n/N	F n/N
0	0/ 5	0/ 5	3/ 5	5/ 5	5/ 5	0/ 5	0/ 5	3/ 5	5/ 5	5/ 5
1	0/ 5	0/ 5	2/ 5	5/ 5	5/ 5	0/ 5	0/ 5	1/ 5	3/ 3	2/ 2
2	0/ 5	0/ 5	0/ 5	5/ 5	5/ 5	0/ 5	0/ 5	0/ 5	2/ 2	2/ 2
3	0/ 5	0/ 5	0/ 5	4/ 5	5/ 5	0/ 5	0/ 5	0/ 5	2/ 2	2/ 2
4	0/ 5	0/ 5	0/ 5	1/ 5	4/ 5	0/ 5	0/ 5	0/ 5	0/ 2	2/ 2
5	0/ 5	0/ 5	0/ 5	1/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2
6	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	1/ 2
7	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
8	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
9	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
10	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
11	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
12	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
13	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 5	0/ 2	0/ 1
14	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0	0/ 0

Legend: n = number of animals with signs, N = survivors

M = males, F = females

Reflexes

Measurements on day: 1 / MALES

Type of Reflex	Group 1	Group 2	Group 3	Group 4	Group 5
Visual placing response	0/5	0/5	0/5	0/5	0/5
Grip strength	0/5	0/5	0/5	1/5	0/5
Tonus	0/5	0/5	0/5	0/5	0/5
Cornea reflex	0/5	0/5	0/5	0/5	0/5
Light reflex	0/5	0/5	0/5	2/5	0/5
Pinna reflex	0/5	0/5	0/5	0/5	0/5
Startle reflex / sound	0/5	0/5	0/5	0/5	0/5
Startle reflex / touch	0/5	0/5	0/5	0/5	0/5
Tail-pinch response	0/5	0/5	0/5	0/5	0/5
Righting response	0/5	0/5	0/5	0/5	0/5

#/#: number of rats showing abnormal reflexes / number of rats investigated

Measurements on day: 1 / FEMALES

Type of Reflex	Group 1	Group 2	Group 3	Group 4	Group 5
Visual placing response	0/5	0/5	0/5	1/3	0/2
Grip strength	0/5	0/5	0/5	1/3	0/2
Tonus	0/5	0/5	0/5	1/3	0/2
Cornea reflex	0/5	0/5	0/5	0/3	0/2
Light reflex	0/5	0/5	0/5	1/3	0/2
Pinna reflex	0/5	0/5	0/5	1/3	0/2
Startle reflex / sound	0/5	0/5	0/5	1/3	0/2
Startle reflex / touch	0/5	0/5	0/5	0/3	0/2
Tail-pinch response	0/5	0/5	0/5	0/3	0/2
Righting response	0/5	0/5	0/5	1/3	0/2

#/#: number of rats showing abnormal reflexes / number of rats investigated

Group 4 / measurements on day 5: all reflexes normal

Körpergewichte / body weights

- I: Expositionstag / exposure day
II: 3. Nachbeobachtungstag / 3rd observation day
III: nach 1 Woche / after 1 week
IV: nach 2 Wochen / after 2 weeks
No.: Tier-Nummer / animal number

Konzentration/concentration: control
Gruppe/group: 1 - sex: MALE

No.	I	II	III	IV
1	209.0	229.0	250.0	279.0
2	208.0	220.0	237.0	266.0
3	210.0	226.0	251.0	294.0
4	197.0	203.0	227.0	257.0
5	187.0	190.0	206.0	227.0
MEAN	202.2	213.6	234.2	264.6
STD	10.0	16.6	18.6	25.2

Alle Gewichte in g / all weights in g

Konzentration/concentration: 75 mg/m³ air
Gruppe/group: 2 - sex: MALE

No.	I	II	III	IV
41	160.0	158.0	175.0	201.0
42	176.0	173.0	199.0	230.0
43	172.0	182.0	208.0	248.0
44	176.0	178.0	204.0	233.0
45	181.0	187.0	211.0	252.0
MEAN	173.0	175.6	199.4	232.8
STD	7.9	11.1	14.4	20.1

Alle Gewichte in g / all weights in g

Körpergewichte / body weights

I: Expositionstag / exposure day
II: 3. Nachbeobachtungstag / 3rd observation day
III: nach 1 Woche / after 1 week
IV: nach 2 Wochen / after 2 weeks
No.: Tier-Nummer / animal number

Konzentration/concentration: 500 mg/m³ air
Gruppe/group: 3 - sex: MALE

No.	I	II	III	IV
21	182.0	170.0	204.0	244.0
22	184.0	166.0	204.0	248.0
23	195.0	184.0	221.0	266.0
24	196.0	182.0	218.0	264.0
25	193.0	193.0	223.0	266.0
MEAN	190.0	179.0	214.0	257.6
STD	6.5	11.0	9.3	10.7

Alle Gewichte in g / all weights in g

Konzentration/concentration: 1500 mg/m³ air
Gruppe/group: 4 - sex: MALE

No.	I	II	III	IV
11	197.0	157.0	173.0	199.0
12	205.0	174.0	209.0	254.0
13	206.0	173.0	198.0	247.0
14	201.0	162.0	171.0	228.0
15	207.0	176.0	198.0	250.0
MEAN	203.2	168.4	189.8	235.6
STD	4.1	8.4	16.9	22.8

Alle Gewichte in g / all weights in g

Körpergewichte / body weights

- I: Expositionstag / exposure day
II: 3. Nachbeobachtungstag / 3rd observation day
III: nach 1 Woche / after 1 week
IV: nach 2 Wochen / after 2 weeks
No.: Tier-Nummer / animal number

Konzentration/concentration: 2500 mg/m³ air
Gruppe/group: 5 - sex: MALE

No.	I	II	III	IV
31	194.0	167.0	182.0	232.0
32	203.0	166.0	179.0	222.0
33	208.0	176.0	196.0	243.0
34	208.0	175.0	195.0	246.0
35	210.0	178.0	199.0	232.0
MEAN	204.6	172.4	190.2	235.0
STD	6.5	5.5	9.0	9.6

Alle Gewichte in g / all weights in g

ONE-WAY ANALYSIS OF VARIANCE OF BODY WEIGHT GAIN

ANALYSIS OF B.W. DATA FOR MALE - OBSERVATION-No.: 1- 2

Group-No.: 1 / control

20.0	12.0	16.0	6.0	3.0
MEDIAN= 12.0	MEAN= 11.4	STD= 7.0		

Group-No.: 2 / 75 mg/m³ air

-2.0	-3.0	10.0	2.0	6.0
MEDIAN= 2.0	MEAN= 2.6	STD= 5.5		

Group-No.: 3 / 500 mg/m³ air

-12.0	-18.0	-11.0	-14.0	.0
MEDIAN=-12.0	MEAN=-11.0	STD= 6.7		

Group-No.: 4 / 1500 mg/m³ air

-40.0	-31.0	-33.0	-39.0	-31.0
MEDIAN=-33.0	MEAN=-34.8	STD= 4.4		

Group-No.: 5 / 2500 mg/m³ air

-27.0	-37.0	-32.0	-33.0	-32.0
MEDIAN=-32.0	MEAN=-32.2	STD= 3.6		

BOX'S TEST FOR HOMOGENEITY OF VARIANCES AT P=.05000 LEVEL

CALCULATED F	D.F.'S	PROBABILITY
.5445	4 & 600.	.7065

HOMOGENEOUS VARIANCES (ONE-TAILED TEST)

ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

SOURCE	SS	DF	MS	F	PROB
TREATMENT	8432.	4	2108.0	67.781	.000
ERROR	622.0	20	31.100		
TOTAL	9054.	24			

OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL

GAMES AND HOWELL MODIFICATION OF
TUKEY-KRAMER'S HONESTLY SIGNIFICANT DIFFERENCE TEST
(WITH THE STUDENTIZED RANGE STATISTIC)

GROUPS COMPARED	CALCULATED TEST VALUE	DEGREES OF FREEDOM	PROBABILITY	CONCLUSION
5. % ONE-TAILED TEST				
1 AND 2	-3.14	8	.2633	NOT SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 2	3.14	8	.2633	NOT SIGNIFICANT
5. % ONE-TAILED TEST				
1 AND 3	-7.31	8	.0055	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 3	7.31	8	.0055	SIGNIFICANT
5. % ONE-TAILED TEST				
1 AND 4	-17.72	7	.0000	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 4	17.72	7	.0000	SIGNIFICANT
5. % ONE-TAILED TEST				
1 AND 5	-17.58	6	.0000	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 5	17.58	6	.0000	SIGNIFICANT
5. % ONE-TAILED TEST				
2 AND 3	-4.97	8	.0460	SIGNIFICANT
5. % TWO-TAILED TEST				
2 AND 3	4.97	8	.0460	NOT SIGNIFICANT
5. % ONE-TAILED TEST				
2 AND 4	-16.90	8	.0000	SIGNIFICANT
5. % TWO-TAILED TEST				
2 AND 4	16.90	8	.0000	SIGNIFICANT
5. % ONE-TAILED TEST				
2 AND 5	-16.88	7	.0000	SIGNIFICANT
5. % TWO-TAILED TEST				
2 AND 5	16.88	7	.0000	SIGNIFICANT
5. % ONE-TAILED TEST				
3 AND 4	-9.39	7	.0018	SIGNIFICANT

5. % TWO-TAILED TEST

3 AND 4 9.39

7

.0018

SIGNIFICANT

5. % ONE-TAILED TEST

3 AND 5 -8.83

6

.0045

SIGNIFICANT

5. % TWO-TAILED TEST

3 AND 5 8.83

6

.0045

SIGNIFICANT

4 AND 5 1.46

8

.8355

NOT SIGNIFICANT

5. % TWO-TAILED TEST

4 AND 5 1.46

8

.8355

NOT SIGNIFICANT

ONE-WAY ANALYSIS OF VARIANCE OF BODY WEIGHT GAIN

ANALYSIS OF B.W. DATA FOR MALE - OBSERVATION-No.: 2- 3

Group-No.: 1 / control

21.0	17.0	25.0	24.0	16.0
MEDIAN= 21.0	MEAN= 20.6	STD= 4.0		

Group-No.: 2 / 75 mg/m³ air

17.0	26.0	26.0	26.0	24.0
MEDIAN= 26.0	MEAN= 23.8	STD= 3.9		

Group-No.: 3 / 500 mg/m³ air

34.0	38.0	37.0	36.0	30.0
MEDIAN= 36.0	MEAN= 35.0	STD= 3.2		

Group-No.: 4 / 1500 mg/m³ air

16.0	35.0	25.0	9.0	22.0
MEDIAN= 22.0	MEAN= 21.4	STD= 9.8		

Group-No.: 5 / 2500 mg/m³ air

15.0	13.0	20.0	20.0	21.0
MEDIAN= 20.0	MEAN= 17.8	STD= 3.6		

BOX'S TEST FOR HOMOGENEITY OF VARIANCES AT P=.05000 LEVEL

CALCULATED F	D.F. 'S	PROBABILITY
1.8987	4 & 600.	.1080

HOMOGENEOUS VARIANCES (ONE-TAILED TEST)

ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

SOURCE	SS	DF	MS	F	PROB
TREATMENT	887.0	4	221.76	7.417	.001
ERROR	598.0	20	29.900		
TOTAL	1485.	24			

OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL

GAMES AND HOWELL MODIFICATION OF
TUKEY-KRAMER'S HONESTLY SIGNIFICANT DIFFERENCE TEST
(WITH THE STUDENTIZED RANGE STATISTIC)

GROUPS COMPARED	CALCULATED TEST VALUE	DEGREES OF FREEDOM	PROBABILITY	CONCLUSION
5. % ONE-TAILED TEST				
1 AND 2	1.80	8	.7124	NOT SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 2	1.80	8	.7124	NOT SIGNIFICANT
5. % ONE-TAILED TEST				
1 AND 3	8.88	8	.0016	SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 3	8.88	8	.0016	SIGNIFICANT
5. % ONE-TAILED TEST				
1 AND 4	.24	5	.9997	NOT SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 4	.24	5	.9997	NOT SIGNIFICANT
5. % ONE-TAILED TEST				
1 AND 5	-1.64	8	.7713	NOT SIGNIFICANT
5. % TWO-TAILED TEST				
1 AND 5	1.64	8	.7713	NOT SIGNIFICANT
5. % ONE-TAILED TEST				
2 AND 3	7.06	8	.0069	SIGNIFICANT
5. % TWO-TAILED TEST				
2 AND 3	7.06	8	.0069	SIGNIFICANT
5. % ONE-TAILED TEST				
2 AND 4	-.72	5	.9825	NOT SIGNIFICANT
5. % TWO-TAILED TEST				
2 AND 4	.72	5	.9825	NOT SIGNIFICANT
5. % ONE-TAILED TEST				
2 AND 5	-3.59	8	.1736	NOT SIGNIFICANT
5. % TWO-TAILED TEST				
2 AND 5	3.59	8	.1736	NOT SIGNIFICANT
5. % ONE-TAILED TEST				
3 AND 4	-4.19	5	.1406	NOT SIGNIFICANT

5. % TWO-TAILED TEST

3 AND 4 4.19

5 .1406

NOT SIGNIFICANT

5. % ONE-TAILED TEST

3 AND 5 -11.42

8 .0002

SIGNIFICANT

5. % TWO-TAILED TEST

3 AND 5 11.42

8 .0002

SIGNIFICANT

5. % ONE-TAILED TEST

4 AND 5 -1.10

5 .9278

NOT SIGNIFICANT

5. % TWO-TAILED TEST

4 AND 5 1.10

5 .9278

NOT SIGNIFICANT

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ONE-WAY ANALYSIS OF VARIANCE OF BODY WEIGHT GAIN

ANALYSIS OF B.W. DATA FOR MALE - OBSERVATION-No.: 3- 4

Group-No.: 1 / control

29.0	29.0	43.0	30.0	21.0
MEDIAN= 29.0	MEAN= 30.4	STD= 7.9		

Group-No.: 2 / 75 mg/m³ air

26.0	31.0	40.0	29.0	41.0
MEDIAN= 31.0	MEAN= 33.4	STD= 6.7		

Group-No.: 3 / 500 mg/m³ air

40.0	44.0	45.0	46.0	43.0
MEDIAN= 44.0	MEAN= 43.6	STD= 2.3		

Group-No.: 4 / 1500 mg/m³ air

26.0	45.0	49.0	57.0	52.0
MEDIAN= 49.0	MEAN= 45.8	STD= 11.9		

Group-No.: 5 / 2500 mg/m³ air

50.0	43.0	47.0	51.0	33.0
MEDIAN= 47.0	MEAN= 44.8	STD= 7.3		

BOX'S TEST FOR HOMOGENEITY OF VARIANCES AT P=.05000 LEVEL

CALCULATED F	D.F.'S	PROBABILITY
1.8837	4 & 600.	.1105

HOMOGENEOUS VARIANCES (ONE-TAILED TEST)

ONE-WAY CLASSIFICATION ANALYSIS OF VARIANCE

SOURCE	SS	DF	MS	F	PROB
TREATMENT	1023.	4	255.70	4.147	.013
ERROR	1233.	20	61.660		
TOTAL	2256.	24			

OVERALL SIGNIFICANCE AT 5.% (ONE-TAILED) LEVEL

GAMES AND HOWELL MODIFICATION OF
TUKEY-KRAMER'S HONESTLY SIGNIFICANT DIFFERENCE TEST
(WITH THE STUDENTIZED RANGE STATISTIC)

GROUPS COMPARED	CALCULATED TEST VALUE	DEGREES OF FREEDOM	PROBABILITY	CONCLUSION
<hr/>				
5. % ONE-TAILED TEST				
<hr/>				
1 AND 2	.91	8	.9628	NOT SIGNIFICANT
<hr/>				
5. % TWO-TAILED TEST				
<hr/>				
1 AND 2	.91	8	.9628	NOT SIGNIFICANT
<hr/>				
5. % ONE-TAILED TEST				
<hr/>				
1 AND 3	5.06	5	.0758	NOT SIGNIFICANT
<hr/>				
5. % TWO-TAILED TEST				
<hr/>				
1 AND 3	5.06	5	.0758	NOT SIGNIFICANT
<hr/>				
5. % ONE-TAILED TEST				
<hr/>				
1 AND 4	3.41	7	.2178	NOT SIGNIFICANT
<hr/>				
5. % TWO-TAILED TEST				
<hr/>				
1 AND 4	3.41	7	.2178	NOT SIGNIFICANT
<hr/>				
5. % ONE-TAILED TEST				
<hr/>				
1 AND 5	4.23	8	.0944	NOT SIGNIFICANT
<hr/>				
5. % TWO-TAILED TEST				
<hr/>				
1 AND 5	4.23	8	.0944	NOT SIGNIFICANT
<hr/>				
5. % ONE-TAILED TEST				
<hr/>				
2 AND 3	4.53	5	.1097	NOT SIGNIFICANT
<hr/>				
5. % TWO-TAILED TEST				
<hr/>				
2 AND 3	4.53	5	.1097	NOT SIGNIFICANT
<hr/>				
5. % ONE-TAILED TEST				
<hr/>				
2 AND 4	2.87	6	.3546	NOT SIGNIFICANT
<hr/>				
5. % TWO-TAILED TEST				
<hr/>				
2 AND 4	2.87	6	.3546	NOT SIGNIFICANT
<hr/>				
5. % ONE-TAILED TEST				
<hr/>				
2 AND 5	3.63	8	.1671	NOT SIGNIFICANT
<hr/>				
5. % TWO-TAILED TEST				
<hr/>				
2 AND 5	3.63	8	.1671	NOT SIGNIFICANT
<hr/>				
5. % ONE-TAILED TEST				
<hr/>				
3 AND 4	.57	4	.9917	NOT SIGNIFICANT

5. % TWO-TAILED TEST

3 AND 4 .57
5. % ONE-TAILED TEST

4

.9917

NOT SIGNIFICANT

3 AND 5 .50
5. % TWO-TAILED TEST

5

.9957

NOT SIGNIFICANT

3 AND 5 .50
5. % ONE-TAILED TEST

5

.9957

NOT SIGNIFICANT

4 AND 5 -.23
5. % TWO-TAILED TEST

7

.9999

NOT SIGNIFICANT

4 AND 5 .23

7

.9999

NOT SIGNIFICANT

Körpergewichte / body weights

I: Expositionstag / exposure day
II: 3. Nachbeobachtungstag / 3rd observation day
III: nach 1 Woche / after 1 week
IV: nach 2 Wochen / after 2 weeks
No.: Tier-Nummer / animal number

Konzentration/concentration: control

Gruppe/group: 1 - sex: FEMALE

No.	I	II	III	IV
6	165.0	163.0	166.0	173.0
7	166.0	166.0	176.0	183.0
8	166.0	167.0	176.0	181.0
9	167.0	169.0	176.0	176.0
10	173.0	176.0	181.0	187.0
MEAN	167.4	168.2	175.0	180.0
STD	3.2	4.9	5.5	5.6

Alle Gewichte in g / all weights in g

Konzentration/concentration: 75 mg/m³ air

Gruppe/group: 2 - sex: FEMALE

No.	I	II	III	IV
46	185.0	186.0	197.0	206.0
47	183.0	180.0	185.0	196.0
48	189.0	184.0	194.0	207.0
49	191.0	185.0	195.0	202.0
50	185.0	183.0	193.0	201.0
MEAN	186.6	183.6	192.8	202.4
STD	3.3	2.3	4.6	4.4

Alle Gewichte in g / all weights in g